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## CHOLECYSTITIS WITH PERFORATION

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IN AN attempt to determine the true incidence of perforation of the gallbladder in a large series of necropsies, a review was made of 12,000 consecutive routine autopsies done at the Los Angeles County Hospital from April 1936 to January 1942. It is evident from the results of this large series of necropsies that the incidence and mortality of perforation of the gallbladder are much higher than heretofore generally believed. The argument for early operation for acute cholecystitis as a means of lowering the mortality from perforation is further strengthened by the presentation of an analysis of 105 cases of acute cholecystitis in which operation was performed at the White Memorial Hospital, Los Angeles, in the period between 1924 and 1944 and at the Glendale Sanitarium and Hospital, Glendale, Calif., in the period between 1927 and 1944.

A vast amount of writing has been done on the subject of acute cholecystitis, but a comprehensive review of the literature covering the last decade indicates that debate is still going on regarding early or delayed operation. The trend in recent years, however, is definitely toward early surgical intervention. Failure of many physicians heretofore to accept early operation as the logical means of limiting the morbidity and lessening the mortality of acute cholecystitis seems to result from a failure to appreciate the incidence and gravity of perforation. Many, it would seem, have been content to risk this "supposedly" infrequent ominous development rather than subject the patient to the "alleged" dangers of an early operation.

We feel that the subject of perforation is of much practical importance, for on its frequency and inherent dangers should rest largely the decision as to the most opportune time to operate for acute cholecystitis. If it can be shown that the incidence and mortality are

high then the brief for early operation is strengthened, and conversely, if perforation of the acutely diseased gallbladder is rare and the mortality low delay in surgical intervention would not be so potentially dangerous.

#### FREQUENCY OF PERFORATION

Considerable data are available in the literature on the incidence of perforation in cases of actual disease of the gallbladder. Cowley and Harkins (1943)<sup>1</sup> have made perhaps the most complete review of the literature on the incidence of perforation, extending from 1924 to 1942 and embracing the data presented by eighteen authors, including also a series of their own of 25 cases of perforated gallbladder. The average of total figures cited in a review of twelve thousand, nine hundred and fifteen operations on the gallbladder showed perforation occurring in 2.8 per cent of the cases. Focusing on acute conditions within the gallbladder, of which there were 2,261 cases, one finds that perforation occurred in 13 per cent. The mortality rate in cases of perforation was 20.8 per cent.

Heuer (1937)<sup>2</sup> concluded from his review of the literature that gangrene and perforation of the gallbladder occurred in 20 per cent of the cases of acute cholecystitis in which the pathologic process was not interrupted by surgical treatment, while his review of the experiences of fourteen authors, citing 500 cases of perforation, showed that the mortality varied between 15 and 65 per cent, averaging 45 per cent.

Perforation itself represents the end result of a progressive pathologic change in the acute condition of the gallbladder, the incidence and seriousness of which, it appears, have not been appreciated. If one judges from the content of earlier papers by Branch and Zollinger,<sup>3</sup> Smith,<sup>4</sup> Cave<sup>5</sup> and others, it would appear that it was felt that perforation was rather unusual or that if it did occur localization would generally be the rule.

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1. Cowley, L. L., and Harkins, H. N.: Perforation of the Gallbladder: A Study of Twenty-Five Consecutive Cases, *Surg., Gynec. & Obst.* **77**:661-668 (Dec.) 1943.

2. Heuer, G. J.: The Factors Leading to Death in Operations upon the Gall-Bladder and Bile-Ducts, *Ann. Surg.* **99**:881-892 (June) 1934; *Surgical Aspects of Acute Cholecystitis*, *ibid.* **105**:758-764 (May) 1937.

3. Branch, C. D., and Zollinger, R.: Acute Cholecystitis: A Study of Conservative Treatment, *New England J. Med.* **214**:1173-1177 (June 11) 1936.

4. Smith, M. K.: The Treatment of Acute Cholecystitis, *Am. J. Surg.* **40**: 192-196 (April) 1938.

5. Cave, H. W.: Immediate or Delayed Treatment of Acute Cholecystitis: Liver Shock and Death, *Surg., Gynec. & Obst.* **66**:308-314 (Feb.) 1938.

Contrary to these, Sanders,<sup>6</sup> Heuer,<sup>2</sup> Hotz,<sup>7</sup> Stone<sup>8</sup> and their colleagues found that perforation without localization was by no means infrequent.

With respect to the appendix, Heuer (1937)<sup>2</sup> cited the incidence of gangrene and perforation in acute appendicitis to be 17.5 per cent in a series of 593 cases as compared with an incidence of gangrene and perforation of 15.7 per cent in a series of acute conditions within the gallbladder observed during the same period, which fact should dispel the contention that acute perforation of the gallbladder is rare when compared with that of acute perforation of the appendix. When this comparison is made, it is interesting to note that Hotz (1939)<sup>7</sup> concluded from his investigations that the incidence of peritonitis associated with perforation of the gallbladder was found to rank as high as that of peritonitis associated with the acute perforation of the appendix, which was reported by McClure and Altemeier,<sup>9</sup> as occurring in 53 per cent of their series of cases.

The surgical significance of this comparison should lead to the definite conclusion that just as surely as the mortality and morbidity rates have been lowered by early operation for acute appendicitis just so must they be lowered by operation for the acutely diseased gallbladder, by an interruption at an early stage of the pathologic process which will so frequently result in the catastrophe of perforation, with its high incidence of fatality.

#### ANALYSIS OF CASES OF PERFORATION

Considerable data appear in the literature on the incidence of perforation in gallbladder disease, but little, comparatively speaking, is found regarding the incidence of perforation of the gallbladder as a cause of death. Our series reviews 12,000 consecutive routine necropsies performed at the Los Angeles County Hospital from April 1936 to January 1942 and reveals 32 instances in which perforated gallbladder was found to be the cause of death, or an incidence of 0.26 per cent. In other words, approximately 1 in every 375 persons succumbed to a perforated gallbladder, surely a much higher incidence than generally heretofore believed.

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6. Sanders, R. L.: Perforation of Gallbladder: Analysis of Forty-Six Cases, *Surgery* 1:949-958 (June) 1937.

7. Hotz, R.: Perforated Cholecystitis, *Am. J. Surg.* 44:706-711 (June) 1939; Acute Cholecystitis with Discussion of Factors in Morbidity and Mortality, *ibid.* 44:695-705 (June) 1939.

8. Stone, W. W.: Perforation of the Gallbladder Occurring in the Late Stage of Pregnancy, *J. A. M. A.* 109:1903-1904 (Dec. 4) 1937.

9. McClure, R. D., and Altemeier, W. A.: Acute Perforated Appendicitis with Peritonitis, *Ann. Surg.* 105:800-814 (May) 1937.

For instance, Karullon, cited by Nix (1940),<sup>10</sup> reported 6,114 consecutive necropsies in only 3 of which death was due to perforation of the gallbladder, whereas our series, showing 1 death due to perforation in every 375 deaths from all causes, should surely dispel the contention that perforation is infrequent, rare or seldom fatal!

*Sex.*—Most series show all types of gallbladder disease to occur with greater incidence in women; however, in this series of cases of perforation, owing to some unknown vagary, 22, or 68 per cent, of the patients were men, while 10, or 31 per cent, were women, a sex ratio quite the reverse of that usually found. A ratio favoring the men occurred in Sanders' (1937)<sup>6</sup> series of 46 perforations of the gallbladder in 22 women and 24 men.

*Age.*—Compilation of table 1 revealed the youngest patient to be 42 years and the oldest 91 years old. The literature shows that by far the majority of perforated gallbladders occur in patients past 50 years. Schaeffer (1942)<sup>11</sup> gave the average age of his 20 patients to be 59 years. In our series, 91 per cent of the patients were past 50 years.

*Duration of Present Illness.*—In the present autopsy series of 32 cases, in 16, or 50 per cent, the onset of the present attack to the time

TABLE 1.—*Age Incidence of Patients with Perforation of the Gallbladder*

| Age, Years | Number of Cases | Percentage |
|------------|-----------------|------------|
| 40-49..... | 3               | 8.1        |
| 50-59..... | 7               | 21.8       |
| 60-69..... | 7               | 21.8       |
| 70-79..... | 10              | 31.2       |
| 80-89..... | 4               | 12.5       |
| 90-99..... | 1               | 3.1        |

of hospitalization did not exceed seven days, while the remainder were of varying or unstated time. However, many of the patients in the former group presented acute pathologic conditions. If they had not been conservatively treated, the condition undiagnosed or misdiagnosed or if early instead of delayed operation had been done, it is felt that a considerable number of lives would have been saved.

*Classification as to Type of Perforation.*—Table 2 compares the incidence of free and localized types of perforations as occurring in our series with the incidence of those tabulated from the literature. Free perforation of the gallbladder with generalized peritonitis (type I of Niemeier) occurred in 42 per cent of our cases, as shown in table 3. This is considerably higher than the incidence found by Cowley and

10. Nix, J. T., in discussion on McCloskey, J. F., and Lehman, J. A.: Surgical Management of Acute Cholecystitis, *Rev. Gastroenterology* 7:176-183 (March-April) 1940.

11. Schaeffer, R. L.: Acute and Chronic Perforations of the Gallbladder, *Pennsylvania M. J.* 45:566-569 (March) 1942.

Harkins (1943),<sup>1</sup> who reported a series of 25 cases, with an incidence of free perforation in 24 per cent. Hotz (1939),<sup>7</sup> however, in reporting a series of 574 cases of acute conditions of the gallbladder, found 69 instances of perforation, or an incidence of 12 per cent. Peritonitis was present in 77 per cent of the patients at the time of operation, and 60 per cent of these presented diffuse or general peritonitis. A bile peritonitis was described in 6 cases, or 17 per cent of our series. These were not confused with a bile-tinged ascitic fluid as found in jaundice, so far as could be determined from available data.

TABLE 2.—Incidence of Free and Localized Perforations of the Gallbladder

| Author  | Year | Cases of Free Perforations |            | Cases of Perforations with Localization |            |
|---|------|----------------------------|------------|---|------------|
|   |      | Number                     | Percentage | Number                                  | Percentage |
| Niemeier, O. W.: Ann. Surg. 99: 922 (June) 1934.                              | 1934 | 2                          | 25.0       | 6                                       | 75.0       |
| Sanders <sup>6</sup> .....  | 1937 | 4                          | 8.6        | 42                                      | 91.0       |
| Pennoyer, G. P.: Ann. Surg. 107: 543 (April) 1938                             | 1938 | 7                          | ....       | ..                                      | ....       |
| Stone, W. W., and Douglas, F. M.: Am. J. Surg. 45: 301 (Aug.) 1939.           | 1939 | 6                          | 35.0       | 11                                      | 64.7       |
| Hotz <sup>7</sup> .....   | 1939 | 53                         | 76.7       | 16                                      | 23.1       |
| Atlee, J. L., and Atlee, J. L., Jr.: Pennsylvania M. J. 44: 731 (March) 1941. | 1940 | 4                          | 26.6       | 11                                      | 73.3       |
| Glenn, F., and Moore, S. W.: Arch. Surg. 44: 677 (April) 1942                 | 1942 | 3                          | 12.0       | 22                                      | 88.0       |
| Schaeffer <sup>11</sup> .....   | 1942 | 14                         | 70.0       | 6                                       | 30.0       |
| Cowley and Harkins <sup>1</sup> .....   | 1943 | 6                          | 24.0       | 19                                      | 76.0       |
| Johnstone and Ostendorph* .....   | 1944 | 14                         | 42.4       | 19                                      | 57.6       |
| Total or average.....   |      | 118                        |            | 152                                     |            |

\* Total cases of perforated gallbladder = 32. Of these, there were 14 cases of free perforation of the gallbladder with generalized peritonitis and 19 cases of localized perforation, 1 case revealing both a free and a localized perforation.

TABLE 3.—Classification of Series of Perforations According to Niemcier

| Type             |  | Number of Cases | Percentage |
|------------------|--|-----------------|------------|
| Type I.          | Acute free perforation with generalized peritonitis..... ("Bile peritonitis" ..... | 14              | 42.4       |
| Type II.         | Pericholecystic abscess with localized peritonitis (subacute) .....                | 14              | 42.4       |
| Type III.        | Biliary fistula (chronic).....   | 5               | 15.1       |
|                  | Into duodenum .....  | 4               |            |
|                  | Into liver* .....  | 1               |            |
| Total cases..... |  | 33*             |            |

\* Total cases = 32. One case, counted twice, had both a free perforation of the gallbladder, with generalized peritonitis, and a perforation into the liver.

It is interesting to note that of the 4 cases of perforation into the duodenum 2 of these also revealed at necropsy a generalized peritonitis due apparently to subsequent perforation of the jejunum in 1 instance and to leakage from an unstated site in the other.

One death, not included in the series of perforated gallbladder, was stated by the surgeon performing the autopsy as being due to acute cholecystitis, cholelithiasis and perforation of the common duct, with

localized peritonitis. Why the perforation was in the common duct rather than in the gallbladder was not clear.

*Incidence of Gallstones.*—Stones were found to be present in 84 per cent of these cases and were not found in 4 cases, or 12 per cent. One instance of spontaneous cholecystoduodenostomy, resulting from extrusion of gallstone into the duodenum, resulted in intestinal obstruction and perforation of the jejunum, with consequent generalized peritonitis. Schaeffer<sup>11</sup> (1942) reported all his 20 patients with perforation, with the possible exception of 1, as having stones.

*Diagnosis and Disposition of Cases.*—As shown in table 4, the 32 cases comprising our series were divided into three groups. It is striking to note that group III, representing the cases in which no diagnosis had been made prior to coming to necropsy, numbered 16, which is 50 per cent of the total series. Touroff (1934)<sup>12</sup> found in a review of 429 cases of cholecystitis that minimal or absent clinical manifestations

TABLE 4.—*Diagnosis and Disposition of Cases of Perforated Gallbladder*

|  | Cases of<br>Conservative Treat-<br>ment (Medically) |            | Cases of Delayed<br>Operation    |            |
|--|---|------------|----------------------------------|------------|
|  | Number  | Percentage | Number                           | Percentage |
| Group I. Pathologic changes in gallbladder diagnosed on patient's admission to hospital  | 6   | 17.6       | 2<br>(cholecystostomies)*        | 5.8        |
| Group II. Suspected pathologic changes in gallbladder diagnosed on admission to hospital | 4<br>(aspiration of mass in 1)                      | 11.7       | 2<br>(exploratory laparotomies)† | 5.5        |
| Group III. Condition undiagnosed prior to necropsy                                       | 15<br>(peritoneoscopy in 1)                         | 47.0       | 2<br>(exploratory laparotomies)† | 5.5        |
| Group IV. Antemortem diagnosis unstated.....   | 1 case  | 2.8        |                                  |            |

\* Definitive surgical treatment (i. e., on the gallbladder).

† Other surgical treatment.

existed in 75 cases of pathologically proved acute cholecystitis. This may partially explain the failure of diagnosis in a large number of the cases in our series, for in the elderly patients, or those past 50 years, in which the incidence and mortality of perforation are greatest, the clinical manifestations are often minimal or even absent. The majority presented an acute exacerbation of a chronic cholecystitis, with a few patients with acute cholecystitis, a considerable number of whom we feel would not have succumbed to perforation had they not been treated medically or conservatively, as were 26, or 81 per cent.

The majority of the cases, as evidenced by the incidence of gallbladder calculi in 84 per cent, represented biliary disease of long stand-

12. Touroff, A. S. W.: Acute Cholecystitis: A Study of Seventy-Five Proven Cases with Subsiding or Subsided Clinical Manifestations at the Time of Operation, *Ann. Surg.* 99:900-913 (June) 1934.

ing. If in these cases there had been an interval cholecystectomy early in the course of the disease, the progressive and irreversible pathologic state, ending with gangrene and perforation, would not have developed.

In 2 cases, delayed operation was instituted, cholecystostomy or simple drainage of an abscess being employed. These 2 cases, or only 6.2 per cent, represent the only definitive surgical treatment done on the gallbladder itself. In 4 other cases, surgical treatment other than definitive operation on the gallbladder was done. In this group are found 4 patients on whom exploratory laparotomies were performed. One was operated on for possible intestinal obstruction, but a perforated gallbladder proved to be the unrecognized pathologic change. (In this case the diagnosis had been acute cholecystitis four months previously, and the patient had been treated conservatively.) The second laparotomy was done for possible intestinal obstruction or acute appendicitis, and a post-operative diagnosis of diverticulitis of the sigmoid was made; the gallbladder was apparently not adequately explored to identify or do anything about the real pathologic changes. The third laparotomy was performed for a suspected perforated peptic ulcer, but instead a perforated gallbladder was found. Operation had been delayed eight days in this case, and the patient was being treated conservatively, even though gallbladder disease had been suspected when the patient was admitted to the hospital. The fourth laparotomy was done after a preoperative diagnosis of acute appendicitis. The postoperative diagnosis was the same plus acute cholecystitis, but, owing to the poor condition of the patient, the gallbladder was not dealt with. A delay of twenty-four hours here may have forfeited this patient's chance to survive, which he might have had if early cholecystectomy had been done.

#### REPORT OF A CASE

A case typical of others in the series review is here presented, illustrating the dangers and inadequacy of a medical or so-called conservative regimen in the presence of acute progressive disease of the gallbladder. It also serves to illustrate the need of educating the lay public as to the potential dangers of chronic cholecystic disease, especially that associated with gallstones, inasmuch as it is generally accepted that the pathologic basis of a perforation of the gallbladder is due in practically every instance to an obstruction of the cystic duct, usually by a calculus, and thus are initiated the ensuing progressive pathologic changes culminating in perforation.

W. M., an elderly, white, obese woman of 69 years, was admitted to the hospital Jan. 3, 1940 and died on January 7. The diagnosis when she was admitted was probable recurring cholecystitis. The subsequent history, obtained from a son, revealed that the patient had gallstones for many years, with episodes of nausea, vomiting and abdominal pain. The present attack began two days before hos-



pitalization and was subsequently followed by severe fever, chills and sweats, with the patient in a stupor for two days.

Physical examination was done by the intern. The temperature was 102.2 F. per rectum. The abdomen was relaxed except for voluntary muscle guarding; no mass was palpable. The patient complained on pressure anywhere, even on the chest. The white blood cell count was 15,700. The intern's diagnosis was impending uremia, chronic cervicitis and fever, of undetermined origin.

On January 3 the blood amylase was 156. The resident physician's impression was uremia. The causation was undetermined.

On January 6 the resident physician made a note regarding the history obtained, which revealed that the patient had been told for many years that she had gallstones and noted that the present attack may have had such a basis but that the definite diagnosis was not made as yet. On January 6 it was noted that the patient had evident jaundice. On January 7 a note from the resident physician read, "Patient died this morning. Cause of death not known." The clinical diagnosis as to the cause of death was hepatic and renal insufficiency secondary to recurrent cholecystitis.

At autopsy these observations were made: The abdominal cavity contained an estimated 3 to 4 cc. of foul-smelling, dark gray, semipurulent fluid. The appendix was retrocecal and was free from any inflammation. The gallbladder contained about one hundred small, faceted stones. The entire mucosa was extremely necrotic. The gallbladder was involved in a mass of omentum and fibrous tissue, which bound it firmly to the under surface of the liver and obscured all relations. The wall was greatly thickened and fibrotic, and there seemed to be a perforation on the anterior surface which led into a walled-off abscess, also containing several stones. The abscess in turn had penetrated into the duodenum through an opening measuring about 3 mm. in diameter. Also, the same abscess had penetrated into the peritoneum through another opening measuring about 3 mm. in diameter. The posterior wall of the gallbladder was extremely necrotic and lay in direct apposition with a large necrotic abscess in the liver, with which it seemed to communicate.

At microscopic examination of the gallbladder, the wall was extremely thick. There was perivascular round cell infiltration. The inner surface showed pronounced polymorphonuclear infiltration, and no epithelium was seen. Exudate from the hepatic abscess contained anhemolytic streptococci, and exudate from the gallbladder contained anhemolytic streptococci.

At autopsy the cause of death was established as chronic cholecystitis, cholelithiasis with perforation, abscesses of liver, acute peritonitis and bronchopneumonia.

*Remarks.*—This was a 69 year old woman treated for five days in the hospital, without a definite clinical diagnosis. She died as a result of a perforated gangrenous gallbladder, but if she had been treated surgically, rather than medically or conservatively, at an early date she might have lived.

#### ANALYSIS OF CASES OF ACUTE CHOLECYSTITIS IN WHICH OPERATION WAS PERFORMED

A series of 105 operative cases of acute cholecystitis is next presented in support of the view held by us that early operation, performed within

forty-eight hours of the onset of an acute attack of cholecystitis, is the logical and an effective means of reducing the mortality in this disease by interruption of the progressive process, which so often may result in the catastrophe of perforation. Moreover, cholecystectomy is felt to be the operation of choice, for when it is employed the pathologic condition is removed, thereby obviating the hazards of a later operation, as is often necessitated by cholecystostomy. Early operation increases the practicability of performing cholecystectomy, for within forty-eight hours the dense adhesions encountered in delayed operation are not yet established and the planes of dissection due to pericystic edema are easily defined.

A series of 56 consecutive cases of acute cholecystitis in which operations were performed at the White Memorial Hospital, Los Angeles, as were available from hospital records between 1924 and 1944, combined with a similar series of 49 cases from the records of the Glendale Sanitarium and Hospital, Glendale, Calif., from 1927 to 1944 (105 in all) were used for this study.

TABLE 5.—*Age Incidence in Operative Cases of Acute Cholecystitis*

| Age, Years    | Number of Cases | Percentage |
|---------------|-----------------|------------|
| 30-39.....    | 11              | 10.4       |
| 40-49.....    | 23              | 21.9       |
| 50-59.....    | 34              | 32.3       |
| 60-69.....    | 18              | 17.1       |
| 70 +.....     | 17              | 16.1       |
| Unstated..... | 2               | 1.9        |

*Age and Sex.*—Of this series, 65 per cent of the patients were past 50 years, and, as seen from table 5, the age group from 50 to 59 years provided 32 per cent of the total. The sex ratio favored the women, and this has been true in most series reported in the literature, again an indication that disease of the gallbladder is commoner in women. However, our autopsy series showed the reverse of this, a vagary for which we have no explanation.

*Duration of Acute Illness.*—The duration of the acute attack or illness, i. e., from its onset to the time of operation, is shown in table 6, the cases being classified into three groups, according to interval of time.

*Gangrene and Perforation.*—In our series of 105 cases, gangrene occurred in 13, or 12 per cent. There was 1 death in this group, or a mortality of 7.6 per cent in gangrenous gallbladder. Perforation occurred only three times, with no deaths.

*Type of Operation.*—Referring to table 6, one will note that cholecystectomy was performed in 86, or 82.8 per cent, of the cases and cholecystostomy in 18, or 17 per cent. It is felt, from our experience,

that cholecystectomy is practically always feasible from both a technical and a clinical standpoint when the patient is operated on within forty-eight hours of onset.

*Mortality.*—The mortality rate for the 105 cases is 8.5 per cent. The mortality for the group in which operation was performed within forty-eight hours is 5.8 per cent, but if allowance is made for the surgical accident a rate of 2.9 per cent obtains. For patients operated on in the period forty-eight hours to seven days, the rate is 8.3 per cent. These figures are at variance with the findings of Bonn and Bachhuber<sup>13</sup> with regard to a similar interval. They found a mortality rate of 19 per cent for patients operated on within forty-eight hours of the onset in a series of 16 cases and a mortality rate for the group operated on in a forty-eight hour to seven day interval of only 7.8 per cent in 64 cases. For comparison with the series of Bonn and

TABLE 6.—*Duration of Present Attack, Type of Operation and Mortality*

| Group      | Time Interval | Number of<br>Cases | Cholecys-<br>tectomy | Cholecys-<br>tostomy | Deaths |            |
|------------|---------------|--------------------|----------------------|----------------------|--------|------------|
|            |               |                    |                      |                      | Number | Percentage |
| I.....     | 0-48 hr.      | 34                 | 25                   | 8                    | 2 *    | 5.8        |
| II.....    | 2-7 days      | 36                 | 30                   | 6                    | 3      | 8.3        |
| III.....   | 7+ days       | 35                 | 31                   | 4                    | 4      | 11.4       |
| Total..... |               | 105                | 86                   | 18                   | 9      | 8.5        |

\* One death was due to a surgical accident, and the patient died on the table, with the operation uncompleted. Allowance for this case makes for a mortality in the forty-eight hour group of 2.9 per cent.

Bachhuber,<sup>13</sup> our lowest mortality is in the forty-eight hour group, which represents practically the same number of cases as in each of our other two groups. It is to be noted that there is a progressive increase of mortality proportionate to the time in delay of surgical intervention.

Our series of operative cases does not represent the work of one or two surgical teams but a series performed by a considerable number of different operators, not all of whom, by any means, were surgical specialists, the number also including general practitioners and occasional surgeons. This undoubtedly raised our mortality figures, but despite this our findings indicate the advisability and safety of early cholecystectomy.

Of the 2 patients who died in the forty-eight hour group, 1 died because of a surgical accident, the patient dying on the table ten minutes after operation was begun, and the other was a bedridden patient, under treatment for beriberi, who had a cardiac condition which

13. Bonn, H. K., and Bachhuber, C. A.: The Surgical Treatment of Acute Cholecystitis, *Am. J. Surg.* 49:447-453 (Sept.) 1940.

would have made operation inadvisable at any time. This patient died fifteen hours following operation, from surgical shock and pulmonary edema. The associated pathologic change plus inadequate preoperative preparation, we feel, explains this second fatality and illustrates the fact that there are always a small group of cases of disease due to associated pathologic changes in which the patients should never be subjected to surgical treatment in any circumstances. Here, as in all cases, individualization is necessary.

Our mortality is lowest in the forty-eight hour group, of 34 cases, or a rate of 2.9 per cent, which compares favorably with the series reported by H. F. Graham and M. E. Hoeffle<sup>14</sup> (1938) of 167 cases of acute cholecystitis, with a mortality of 3.5 per cent in patients subjected to operation within forty-eight hours.

#### SUMMARY AND CONCLUSIONS

1. There were found 32 instances of perforation of the gallbladder in a review of 12,000 consecutive routine necropsies done at the Los Angeles County Hospital from April 1936 to January 1942, giving an incidence of 0.26 per cent, or, in other words, in approximately 1 of every 375 cases coming to necropsy death was from a perforated gallbladder. Perforation of the gallbladder as a cause of death has heretofore been given little study in the literature, and these findings should dispel the contention that perforation is infrequent, rare or seldom fatal. Its true incidence places the acutely diseased gallbladder high on the list of potentially fatal conditions as found in acute conditions within the abdomen.

2. The inherent danger of peritonitis following perforation is a real one, and our group of 14 cases of free perforations with acute generalized peritonitis (Niemeier's type I) and 19 of localized perforation indicates that the perforation was not "walled off" in 43 per cent of the cases. This disproves the belief that free perforation is infrequent or that if it occurs it is generally "walled off."

3. The dangers of so-called medical, or conservative, treatment of acute cholecystitis are again emphasized, in that in 49 per cent of the total number of cases the conditions went on to perforation and death, being unrecognized and undiagnosed until necropsy.

4. Once the diagnosis of acute cholecystitis is made, particularly in elderly patients (past 50 years), surgical intervention as early as is consistent with adequate preparation of the patient and operating facilities should take place.

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14. Graham, H. F., and Hoeffle, M. E.: Acute Cholecystitis: Results of Operation Within Forty-Eight Hours of Onset of Symptoms, *Ann. Surg.* **108**: 874-876 (Nov.) 1938.

5. Interval cholecystectomy should be done in cases of recurrent chronic cholecystitis, thereby removing the possibility and dangers of progressive disease.

6. Early operation within forty-eight hours, employing cholecystectomy, is regarded as the logical and effective means of lowering the mortality in acute cholecystitis, the importance of adequate preoperative preparation and evaluation of the operative risk always being remembered.

7. A mortality rate of 2.9 per cent for patients operated on within forty-eight hours compares favorably with the findings of other proponents of early operation and leads to the conclusion that early surgical intervention will lower the mortality from acute perforated cholecystitis just as surely as it has lowered the mortality from acute perforative appendicitis, i. e., by removing the pathologic process before it has progressed to the stage of gangrene and perforation. The findings in 105 cases of acute cholecystitis in which operation was performed show that mortality increases in proportion to the time of operative delay.

# REMOVAL OF SHELL FRAGMENT FROM LEFT VENTRICLE OF THE HEART

Report of a Case

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AND

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MEDICAL CORPS, ARMY OF THE UNITED STATES

THE presence of a foreign body in the myocardium creates a dramatic and challenging situation. If the immediate needs of operation, such as cardiac tamponade, pericarditis or clotted hemothorax, are not present to clearly define surgical intervention, the question of surgical treatment is likely to harass the decision of the surgeon. Intracardiac foreign bodies have not been sufficiently frequent to establish a clear set of rules. As a result, the proverbial two schools of thought have not as yet merged. However, to date, opinion seems to favor removal or attempt at removal. Beck<sup>1</sup> urged the extraction of foreign bodies from the pericardial cavity or myocardium as early as possible and stated that the lapse of time does not mitigate against surgical intervention, even though clinically the patient shows improvement. (The improvement will invariably also be reflected in serial electrocardiograms.) While it is true that a foreign body in the cardiac muscle can become fixed by fibrous tissue, exploration is nevertheless recommended. Davies and Coope<sup>2</sup> held to the same opinion. In cases in which cardiorrhaphy for compression is indicated, they advised removal of the foreign body if it lies superficially and further recommended that "deeply embedded foreign bodies and those in the cavity of the heart are best left until later." A. Tudor Edwards<sup>3</sup> included in his indications for cardiac operation "the presence of foreign bodies, more particularly irregular shell fragments, impacted in the pericardium, in the walls of the heart, or within cavities of the heart."

The dangers of permitting a foreign body to remain in the musculature of the heart are threefold: (1) cardiac rupture, (2) migration into the adjacent cavity, with embolus formation or interference with the

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1. Beck, C. S.: *Surgery of the Heart and Pericardium*, in Christopher, F.: *A Textbook of Surgery*, Philadelphia, W. B. Saunders Company, 1942, p. 1014.

2. Davies, M. H., and Coope, R.: *War Injuries of the Chest*, Edinburgh, E. & S. Livingstone, 1942, p. 103.

3. Edwards, A. T.: *Wounds of the Thorax*, in Bailey, H.: *Surgery of Modern Warfare*, ed. 2, Baltimore, Williams & Wilkins Company, 1942, vol. 1, p. 385.

capacity or function of the chamber, and (3) injury to a coronary vessel.

There are physicians, however, who would take a more conservative view. Bland<sup>4</sup> reported 8 cases of foreign bodies in and about the heart that were not removed. An analysis of these cases, however, affords no definite conclusions, for a sufficiently long enough time has not elapsed for the complete evaluation of the cases. In 1 instance of a bullet lodged within the right ventricle, the patient was experiencing substernal pain five months after the injury, with a sense of pressure radiating to the right upper arm, lasting for one to two hours and unaffected by motion, position or respiration. In another case, after an unsuccessful search for a foreign body in the left ventricle was made, the patient was still experiencing dyspnea on effort six weeks following injury. In all cases, however, the fact that the foreign bodies were permitted to remain, without immediately endangering the lives of the patients, does not serve to prove that such a course is the general procedure of choice and that later sequelae will not ensue.

The management of intracardiac foreign bodies will finally rest on principles evolved from a statistical analysis of the cases in which the patients were operated on and those in which the foreign bodies were left embedded. The present case report is offered as one to be considered for the ultimate over-all study.

#### REPORT OF A CASE

On the morning of June 24, 1944, just outside of Cherbourg, France, a 23 year old American soldier was lying in the prone position, waiting for the signal to move ahead. The signal was given, and the soldier was in the process of getting up when a mortar fragment stung him through his back. He continued to walk, however. He traversed 100 yards (274.32 meters) before he began to feel dizzy; then he experienced transient blindness, which, he believed, persisted for five minutes. He fell to the ground and became extremely dyspneic. Within fifteen minutes he was discovered by a company aid man and was started back through the chain of medical evacuation, receiving plasma, sulfadiazine, tetanus antitoxin, whole blood transfusions and penicillin in the advanced units. At the field hospital the same day, his respiratory distress was relieved by aspiration of 1,580 cc. of whole blood from the left side of the chest. The following day a good deal of mucus was aspirated from the trachea through an endotracheal tube. Tap of the chest at this time yielded only 20 cc. of blood. He was given another transfusion and kept under observation. Combined penicillin and sulfadiazine therapy was maintained. Still another attempt at aspiration, the ensuing day, proved fruitless.

When the patient was first seen by our department, he presented the appearance of a well built person who was cyanotic, slightly dyspneic and ill looking. He had been coughing up some old and fresh blood for the past few days and had begun to have a septic temperature reaching 102 F. He complained of attacks of vertigo

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4. Bland, E. F.: Foreign Bodies in and About the Heart, *Am. Heart J.* 27:588 (April) 1944.

and inability to breathe freely. Blood pressure prior to surgical treatment was 126 systolic and 60 diastolic. Examination of the chest revealed a wound of entrance at the left seventh interspace, paravertebrally (fig. 12), no wound of exit and the classic signs of fluid in the chest, occupying practically the entire



Fig. 1.—Roentgenogram taken July 21, 1944. In this view the foreign body is obscured by a massive left-sided hemothorax.

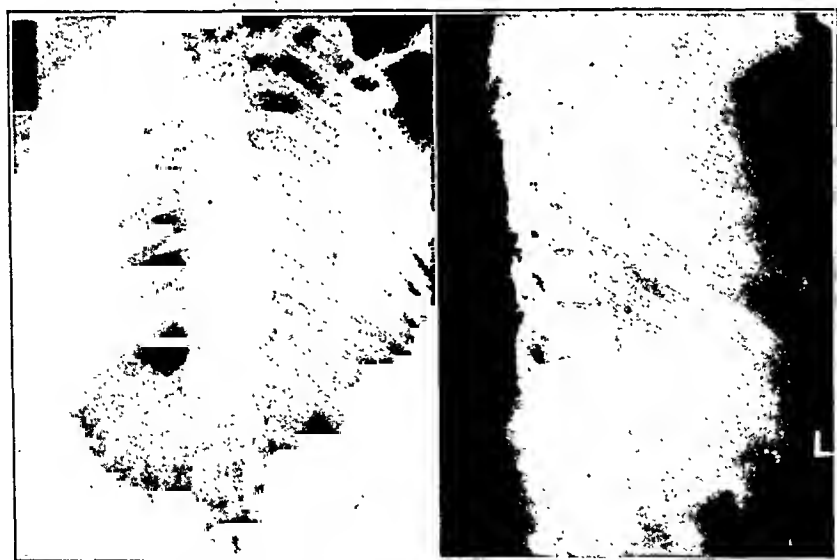


Fig. 2.—Overpenetrated roentgenograms taken July 21, 1944, showing the metallic fragment.

left side of the thorax. Thoracentesis secured only a few cubic centimeters of clotted blood, a culture of which was negative. A diagnosis of clotted hemothorax was made and was supported by roentgenologic observations (fig. 1).



The roentgenograms presented some interesting features. Inasmuch as the initial roentgenograms showed no foreign body because of overshadowing by the hemothorax (fig. 1), overpenetrated plates were made and they revealed a foreign body in the middle of the mediastinum in relationship to the fifth rib anteriorly, about 2.5 cm. to the left of the midline (fig. 2). Capt. M. Rakofsky, Chief of X-Ray Service, further stated that fluoroscopic study seemed to indicate that the foreign body had cardiac motion. This, at the time, however, seemed illogical, inasmuch as the shell fragment had entered from the back and in a line that would have had to traverse the posterior wall as well as the chamber of the left ventricle in order to reach the apical position it now occupied. It appeared that the shell fragment was lodged in an inactivated portion of the lung, adjacent to the apex of the heart, and hence was receiving its motion by transmission. It was only after operation that it became evident how uniquely the fragment had ricocheted to its terminal position. Moreover, on retrospect, it is noteworthy that the blurred appearance of the foreign body (fig. 2) is in distinct contrast to the well defined edges of foreign bodies lodged in pulmonary or muscle tissue, when the roentgenograms are taken during inspiration. This feature is made particular notice of inasmuch as it might prove of diagnostic value in future considerations.

On July 27, 1944, with the patient under endotracheal anesthesia, operation was done, primarily to evacuate the left side of the thorax of clotted blood and secondarily to remove the foreign body. We were assisted by Major Frederick Steele. A transverse incision was made over the anterior aspect of the fifth rib, a portion of which was resected. Later, in order to provide greater exposure, the fourth left costocartilage was cut.

When the thoracic cavity was opened, an enormous amount of clotted blood and large pieces of well organized blood clot as well as sanguinous and sero-sanguinous fluid were removed. This procedure required a good deal of time. After its completion, exploration was carried out. The diaphragm was found to be elevated to the fifth rib and was covered with a fibrinous exudate about 4 mm. thick; the entire pleura, visceral and parietal, was similarly affected. Both lobes of the lung were completely collapsed, and, because the adherent, membranous exudate enveloped the heart and lungs in a continuous fashion, it was impossible to distinguish the one organ from the other.

After decortication of the lung, a cleavage line was established between the lung and heart and complete separation effected. An examination of the lung at this time failed to reveal the presence of a foreign body. It became apparent that the shell fragment, entering posteriorly, had cut through the lung, had struck and reflected from the anterior thoracic wall and had penetrated the heart. The site of entrance, the hemothorax, the burn marks of the missile in the lung tissue and a searing of the cardiac pleura gave evidence of this.

Although the prime purpose of the operation had been effected, it was deemed advisable to search for the foreign body. The condition of the patient was satisfactory. Secondary intervention would be complicated by the formation of adhesions, would be permissible only after a long convalescence and, indeed, might not be possible at all, depending on the type of convalescence the patient would undergo. Infection, though potential, had been staved off by chemotherapy and did not, at the moment, constitute a contraindication. The incision, therefore, was extended toward the midline, and, as was stated previously, the fourth costochondral junction was severed. The pericardium, which was about 2 mm. thick, was opened; it did not contain any fluid. If there had been any degree of hemopericardium, by this time either it had resorbed or the fluid had escaped through a temporarily patent laceration of the pericardium.

Palpation of the myocardium through the pericardial window revealed an elevated surface at the apex. The window was enlarged in order that this area might be visualized; a seared, friable, slightly necrotic myocardium presented itself about 2 cm. from the apex, in the left ventricle. Two chromic no. 1 surgical gut sutures were placed in the apex as tension and subsequent hemostatic sutures. A quick stab wound was made over the foreign body and a small hemostat inserted into the musculature to grasp it. The hemostat sank into the tissue for a distance of about 1.5 cm. and grasped the foreign body, which was immediately withdrawn.

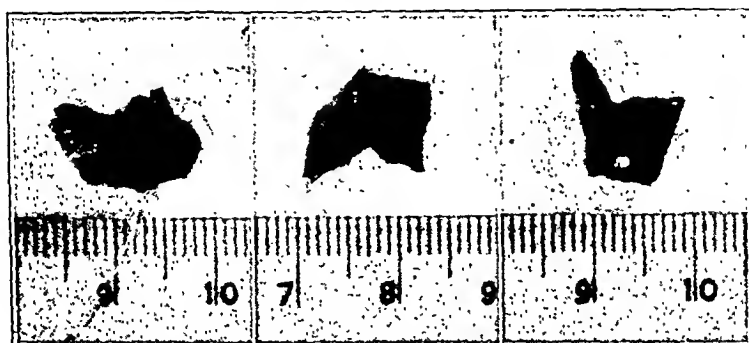


Fig. 3.—Three views of the shell fragment.

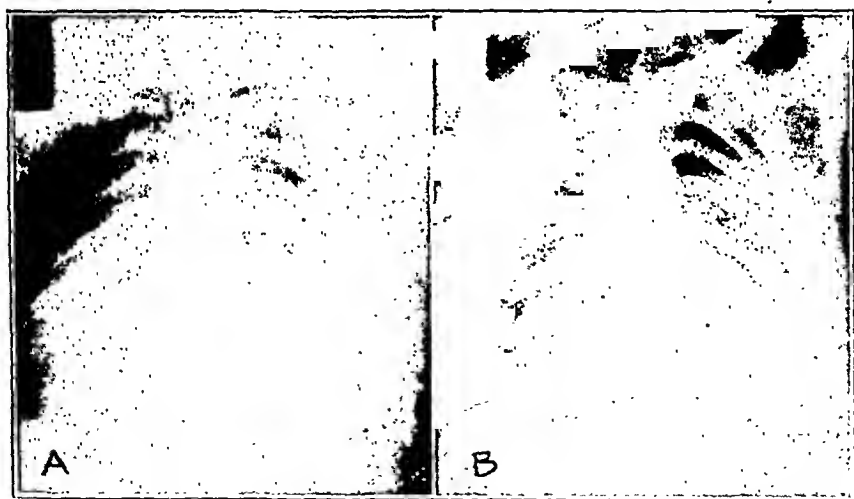


Fig. 4.—Roentgenograms of the patient in the anteroposterior position, taken with portable apparatus. *A*, three days after operation. The cardiac shadow is globular in shape and is displaced to the right. *B*, ten days after operation. The left cardiac border can now be identified.

It proved to be an irregular piece of shell fragment, with jagged edges, measuring 1.5 cm. by 1.2 cm. by 0.6 cm. (fig. 3). Concomitant with the stab wound, spurting bleeding ensued. After removal of the shell fragment, tying of the tension sutures helped control some of the bleeding, and, while traction was still maintained by them, two more sutures were inserted, producing complete hemostasis. The

pericardium was then irrigated with warm isotonic solution of sodium chloride, suctioned and closed, a window being left at the apical region for escape of whatever fluid might subsequently accumulate. Attention was then directed toward the closure of the thoracic wall, which was effected with waterseal, trap bottle drainage.

The patient was under anesthesia for one hour and forty-five minutes; the operation itself required one hour and ten minutes. The patient received 3 units of plasma during the operation and 600 cc. of whole blood immediately on return from the operating room, followed by 1,000 cc. of 5 per cent dextrose in isotonic solution of sodium chloride by hypodermoclysis and, later, a second 1,000 cc. intravenously. Oxygen, sulfadiazine and penicillin therapy were initiated at once, and an additional 500 cc. of whole blood was given the first postoperative day. Two hours after the operation the patient was taking fluids by mouth. His blood pressure was 130 systolic and 70 diastolic and gradually became stabilized at 116 systolic and 60 diastolic; in a few days it fell to 110 systolic and 60 diastolic, at which level it has since more or less remained.

About six hours after operation, a pericardial friction rub, audible over the right costocartilage area of the fourth rib developed. This lasted for about four hours and did not reappear. On the tenth day postoperatively, however, a blowing systolic murmur became evident over the third interspace, 2 cm. to the right of the midline; it occurred in no other region. The murmur diminished progressively and by the fifteenth postoperative day was entirely gone. With the exception of these two incidents, there have been no cardiac abnormalities discernible by physical examination.

Early postoperative complications of cardiac tamponade (due to nondraining pericarditis), atelectasis or pneumonia were watched for carefully but, fortunately, did not appear. Expansion of the left lung proceeded at a rapid rate (fig. 4). Of interest was the pronounced fulness of the right cervical vessels, indicating the shift and fixation of the mediastinum to that side. This was particularly noteworthy inasmuch as the right cervical region assumed an angulation of 90 degrees, in pronounced contrast to a smooth left cervical curvature at the juncture of the neck and shoulder region. This sign persisted until about the fifteenth postoperative day.

Serial electrocardiograms were taken from the day of operation (figs. 5 to 10). The cardiologist, Capt. Ellis W. Young, summarized them as follows:

"The essential changes noted in the records occurred in the ST segments and T waves. Tracings taken soon after operation showed elevated ST segments and small diphasic T waves. Later, as the ST segments approached the base level, coving was present and the T waves became inverted. In the final electrocardiogram the ST segments were isoelectric; the T waves were low and upright in leads I, II and III and inverted in lead IV F. These progressive variations are similar to those associated with pericarditis and are considered to represent the repair of a lesion of the myocardium following surgical treatment of the heart."

The sedimentation rate was 52 mm. per hour the first day postoperatively. By August 8, twelve days postoperatively, it was 11 mm. per hour. A final sedimentation rate, taken November 20, was 2 mm. per hour.

Except for a preoperative secondary anemia of 3,820,000 red blood cells and a 75 per cent hemoglobin content, which was overcome by transfusions, blood picture studies were of no special significance.

Six weeks following operation, the patient was permitted out of bed and graduated exercises were begun. Special exercises were

instituted early to assist in the reexpansion of the lung, to prevent deformity and to aid in the development of the thoracic cage. These exercises were carried out regularly four times daily, under the guidance of Lieut. Dora Dykins, the physical therapist, and were correlated with

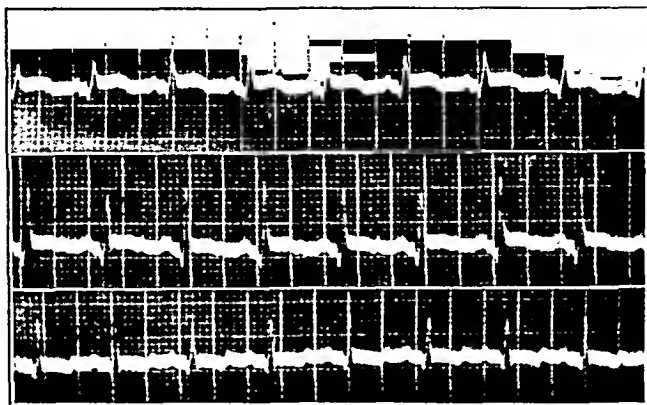


Fig. 5.—Electrocardiogram taken the first day postoperatively. The rate is 125, the P-R interval 0.12 seconds and the QRS interval 0.06 seconds. There are a slight elevation of the S-T segments and low voltage diphasic T waves.

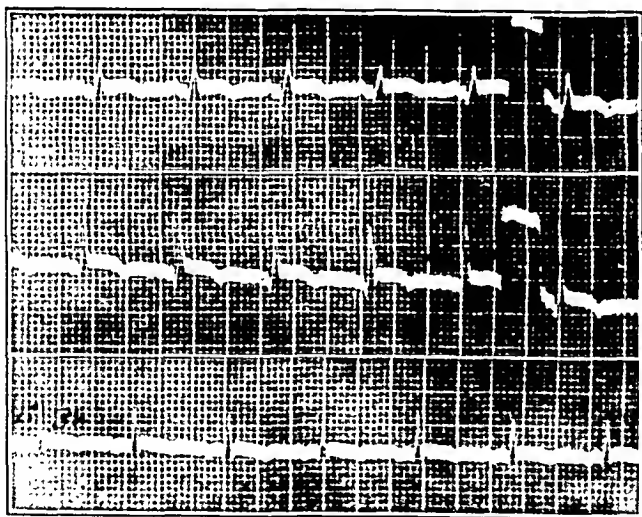


Fig. 6.—Electrocardiogram taken July 31, four days after the operation. The rate is 107, the P-R interval 0.10 seconds and the QRS interval 0.06 seconds. The T waves are low and are diphasic in lead I and inverted in leads II and III. The S-T segments are slightly elevated.

repeated flourosopic examinations. The value of such exercises cannot be overemphasized.

At the time of this writing, four months after operation, the patient is in excellent condition, has no complaints and no deformity of the

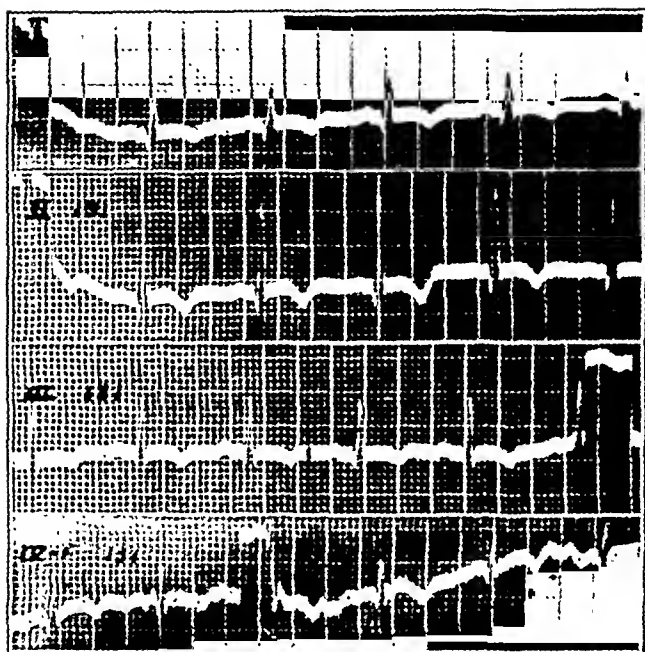


Fig. 7.—Electrocardiogram taken August 28, one month after the operation. The rate is 88, the P-R interval 0.14 seconds and the QRS interval 0.08 seconds. The T waves are inverted. The S-T segment is slightly elevated in leads I and II and isoelectric in lead III.

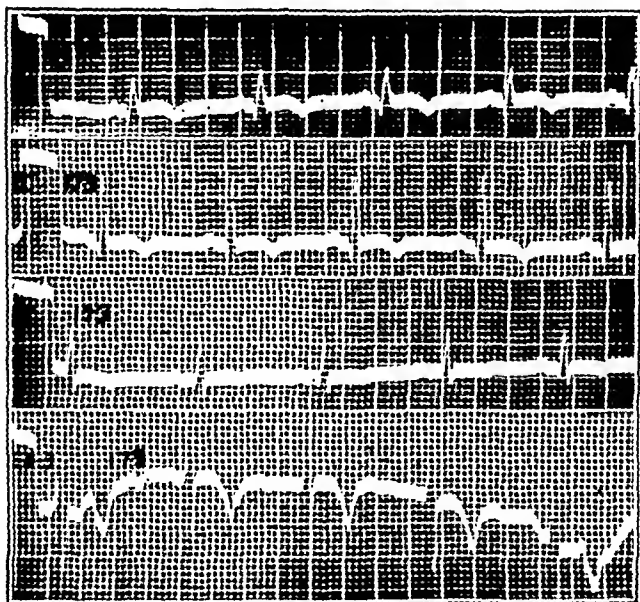


Fig. 8.—Electrocardiogram taken September 14. The rate is 80, the P-R interval 0.14 seconds and the QRS interval 0.08 seconds. The T waves are inverted in leads I, II and IV F and low and diphasic in lead III. The S-T segments are slightly elevated in lead I and isoelectric in leads II, III and IV F.

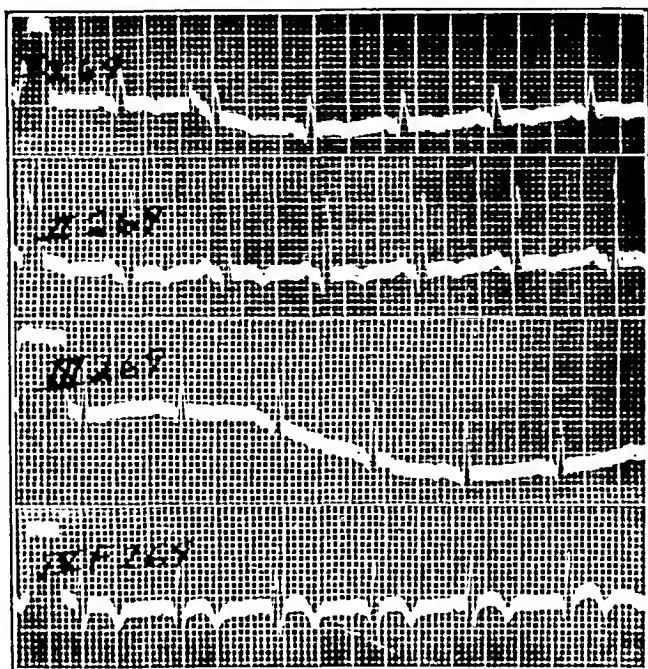


Fig. 9.—Electrocardiogram taken October 19. The rate is 105, the P-R interval 0.14 seconds and the QRS interval 0.07 seconds. The T waves have a lower voltage; they are inverted in leads I, II and IV F and diphasic in lead III. The S-T segments are practically isoelectric.

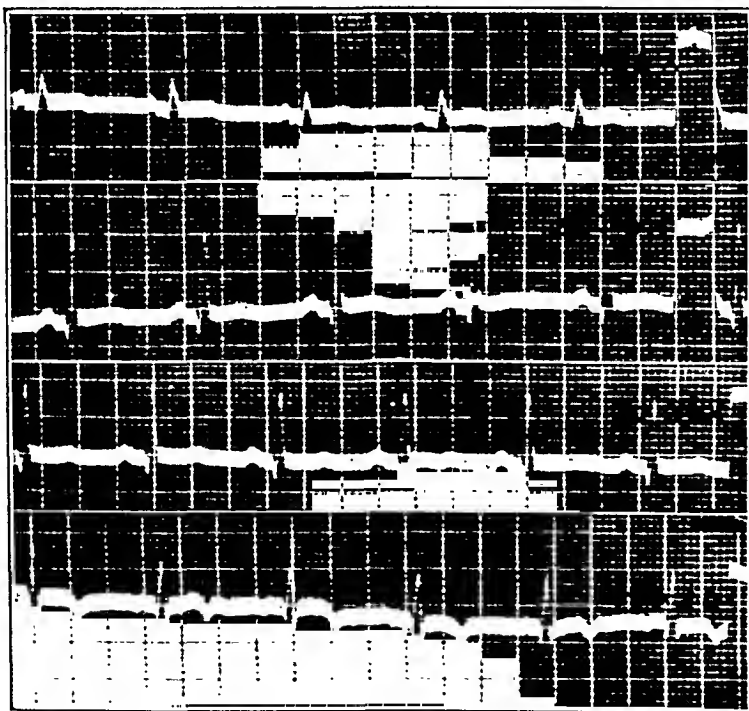


Fig. 10.—Electrocardiogram taken November 28, four months after operation. The rate is 84, the P-R interval 0.14 seconds and the QRS interval 0.08 seconds. The T waves are low and upright in leads I, II and III and inverted in lead IV F.

thoracic wall (fig. 12) and leads a completely independent sedentary existence, with progressive effort tolerance. His blood pressure is maintained at 110 systolic and 64 diastolic; the electrocardiograms indicate progressive improvement (fig. 10), and fluoroscopic follow-ups demonstrate continued improvement in the illumination of the lung



Fig. 11.—Roentgenogram taken November 28. The cardiac shadow is in the midline and is small. Lung fields show normal illumination except for some "streaklike" atelectatic markings of the lower left lobe. The left diaphragm is moderately elevated.



Fig. 12.—Pictures of patient taken three and one-half months after the operation, showing a well rehabilitated thorax. The wound of entrance is seen in the posterior view.

fields and in the motion of the costal cage and diaphragm. The heart is small, is normal in configuration and position (fig. 11) and shows good pulsation on fluoroscopic examination.

SUMMARY AND CONCLUSIONS

1. A case of successful removal of a shell fragment from the left ventricle of the heart is reported.

2. The value of overpenetrated roentgenograms and fluoroscopic examination in locating the foreign body, together with the definity of its edges as a diagnostic value, are noted.

3. Stress is laid on the importance of early and constant exercises for the rehabilitation of the chest.

4. Serial electrocardiograms showed progressive improvement of the myocardial lesion.

Captain Rakofsky, Captain Young and First Lieutenant Dykins, Medical Corps, Army of the United States, gave valuable assistance, and Technician Fifth Grade Charles H. Snyder, Medical Department, Army of the United States, aided with the photography for this article.



## RECONSTRUCTIVE OTOPLASTY

Further Observations; Utilization of Tantalum Wire Mesh Support

CAPTAIN PAUL W. GREELEY (MC), U.S.N.R.

THE reproduction of an auricular cartilage still remains the greatest problem in the construction of a new ear. In an earlier paper,<sup>1</sup> personal experience with Gillies' method, utilizing a maternal ear cartilage as the architectural support around which to build a new ear, was described in detail. Subsequently, a total of fifteen ears were constructed by this procedure. At first, it appeared that this contribution, as described first by Gillies,<sup>2</sup> was a great step in the successful construction of this persistently difficult plastic operation. However, as time progressed, it became apparent that these transplanted auricular cartilages were not going to remain in their original conditions permanently. In each case, the individual cartilage underwent aseptic necrosis and was replaced by fibrous tissue. By and large, this transition developed in one and one-half to two years in small children and in six months to one year in patients of adolescent age. Consequently, with the fibrous tissue replacement, the inevitable contracture typical of all scar tissue ensued and the resulting ear shrank to a small irregular structure. Thus resulted an ear which was unsatisfactory to both the patient and the surgeon. When this fate was discussed with Gillies,<sup>3</sup> it was learned that his end results had been identical with those of my colleagues and me.

Just why the transplanted fresh isografts of auricular cartilage have undergone absorption is not clearly understood. Isografts of costal

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From the Division of Plastic Surgery, United States Naval Hospital, Oakland, Calif.

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This article has been released for publication by the Division of Publications of the Bureau of Medicine and Surgery of the United States Navy. The opinions and views set forth in this article are those of the writer and are not to be construed as reflecting the policies of the Navy Department.

1. Greeley, P. W.: *Reconstructive Otoplasty, Surgery* 10:457-462 (Sept.) 1941.

2. Gillies, H. D.: *Reconstruction of the External Ear, Rev. de chir. structive*, October 1937, pp. 169-179.

3. Gillies, H. D.: Personal communication to the author.

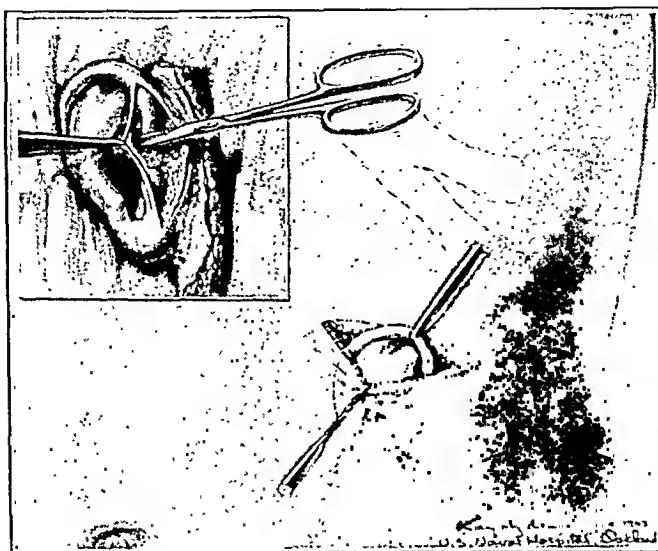


Fig. 1.—The insert in the upper left corner shows the cartilage being dissected from its overlying skin, the ear being entirely avulsed. Below is seen the pocketing of the cartilage in the anterior part of the abdominal wall. (Reproduced by the permission of the *United States Naval Medical Bulletin* 42:1323-1325 [June] 1944.)

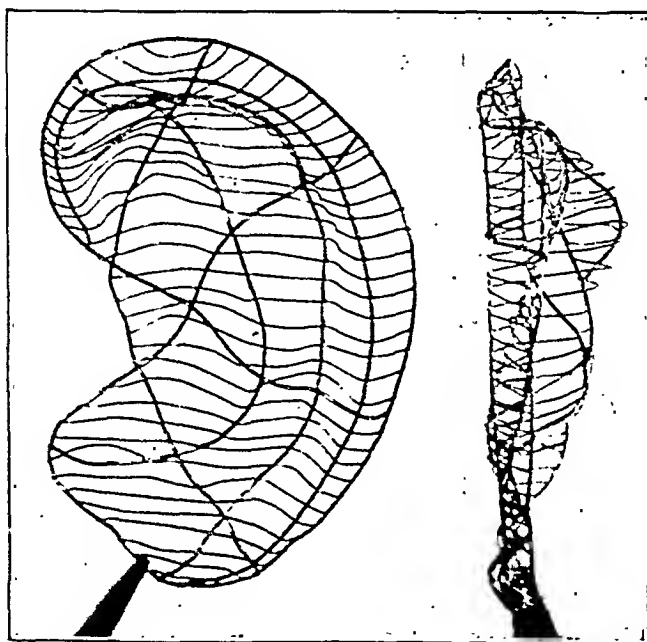


Fig. 2.—Two views of wire mesh model of ear.



Fig. 3.—Areas in temporomastoid skin covered with razor grafts to establish complete healing.



Fig. 4.—Operation showing burial of tantalum wire auricular cartilage mold beneath temporomastoid skin flap and coverage with stent graft.

cartilage on the whole behave satisfactorily. Likewise, transplantation of segments of the conchal portion of the cartilage to reconstruct a subtotal loss of the helix (homograft) is universally successful. Because of this behavior of homografts of auricular cartilage, it was suggested<sup>4</sup> in a previous paper that when one is confronted with a reasonably fresh

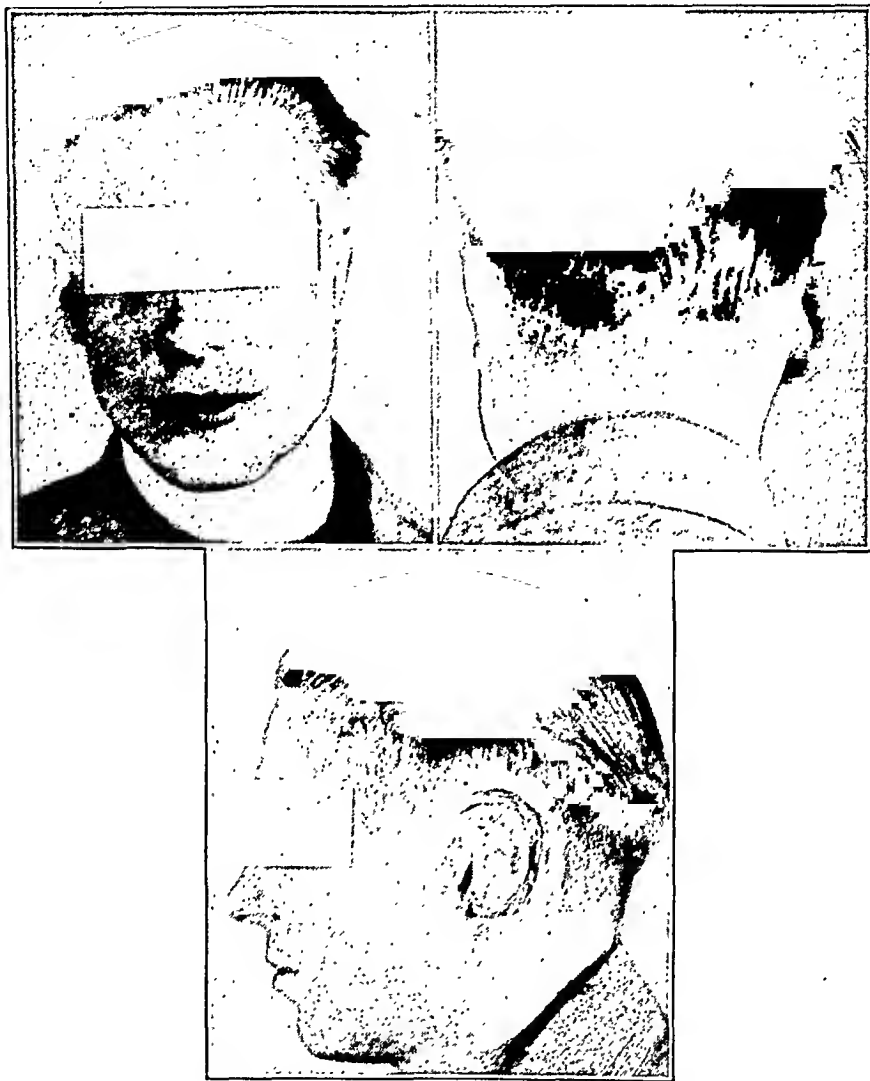


Fig. 5.—Result of operation shown in figure 4.

avulsion of all or part of an ear the cartilage should be preserved and buried subcutaneously until plastic reconstruction is started (fig. 1). While I have never had the opportunity to utilize this procedure, its theoretic application warrants special mention.

4. Greeley, P. W.: Reconstruction of the External Ear: Conservation of the Avulsed Portion, U. S. Nav. M. Bull. 42:1323-1325 (June) 1944.

Other workers have made further contributions. Lamont,<sup>5</sup> in his paper, suggested the use of cartilage from a cadaver ear. In view of the foregoing experience, it would not seem likely that this method would be of success when a fresh isograft of auricular cartilage did not remain in its transplanted state permanently. Furthermore, neither Lamont nor other workers have described a case in which this method was actually carried out. Peer<sup>6</sup> described his method of using diced costal cartilage chips held together in a vitallium ear mold until fibrous tissue proliferation held the mass together. This excellent piece of work has promise.

#### USE OF TANTALUM

In the search for a better support, it was felt that the use of a tantalum frame might be practical. It is realized that tantalum is still a foreign body, but since it has been used successfully in a wide series of cases chiefly by orthopedic surgeons and neurosurgeons its apparent minimal reaction made its use seem worthy of trial in reconstructions of ears.

Through the cooperation of an engineer, Mr. Park B. Hyde, of the Fansteel Corporation, various models of ear cartilages were constructed. We eventually selected a fine wire mesh model, which not only was lighter but would permit development of circulation between the open spaces. These reproductions were made from a model of the normal ear. The wires were then shaped over a negative model by hand and the various pieces secured together by spot welding (fig. 2).

#### DESCRIPTION OF CASE

Our experience deals with only 1 actual case, but the result to date has been so satisfactory that it seems worthy of record for the benefit of persons who have not had an opportunity to see the patient.

An Aviation Ordnance Mate third class, aged 23, was struck and dragged by a station wagon, causing a complete avulsion of the left external ear and much of the adjacent surrounding normal skin. On admission to our service, three months after injury, three small granulating areas in the temporomastoid skin were covered with razor grafts to establish complete healing (fig. 3). In view of the amount of scarring in this area, the vascularity of the skin covering was extremely poor. Consequently, it was necessary to "delay" the primary skin flap six times before development of an adequate circulation was obtained in its base.

When the temporomastoid skin flap had sufficient vascularity, the tantalum wire mold of auricular cartilage was buried beneath it (fig. 4, part 2), after which the borders of the skin were sutured together. Primary healing ensued,

5. Lamont, E. S.: *Reconstructive Plastic Surgery of Absent Ear with Necrocartilage: Original Method*, Arch. Surg. **48**:53-72 (Jan.) 1944.

6. Peer, L.: *Reconstruction of the External Ear with Diced Cartilage Grafts*, Tr. Am. Soc. Plastic & Reconstruct. Surg., 1943, p. 11-16.

and the mold was permitted to remain untouched for seven months. This long interval was allowed so that one might be reasonably certain that no foreign body reaction might occur in this superficial location of relatively poor vascularity.

At the next stage, the curved incision in the skin flap was reopened, being dissected downward behind the transplanted tantalum frame, but carefully so as not to expose any segment of metal wire from the mass of fibrous tissue that had grown around the new support. The structure was then brought forward and the posterior surface of the new ear and the temporomastoid bed covered with a

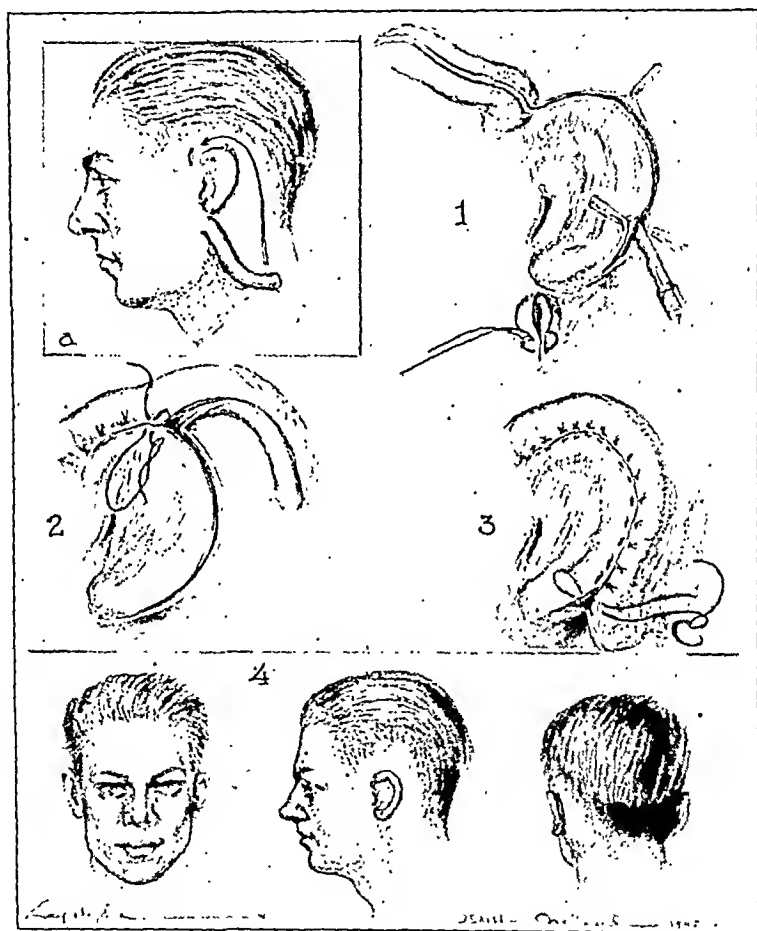


Fig. 6.—Operation showing addition of small tube pedicle flap.

stent graft such as has been described in other standard procedures (fig. 4, part 4). The final result is demonstrated in the artist's sketch (fig. 4, part 5) and by photographs in figure 5.

The new ear was followed closely, because it was felt that, although the procedure might have merit, complications might develop in this particular case because of the extensive fibrosis in both the anterior and the posterior coverings of the skin. Subsequently, after three months of complete healing and absence of reaction, two small areas of pressure

necrosis developed around the peripheral margin. After these areas were observed for six weeks, it seemed apparent that they developed because of scar contracture of the anterior and posterior coverings of the skin over the rigid periphery of the tantalum mold. However, no infection or other inflammatory reaction developed around the open areas.

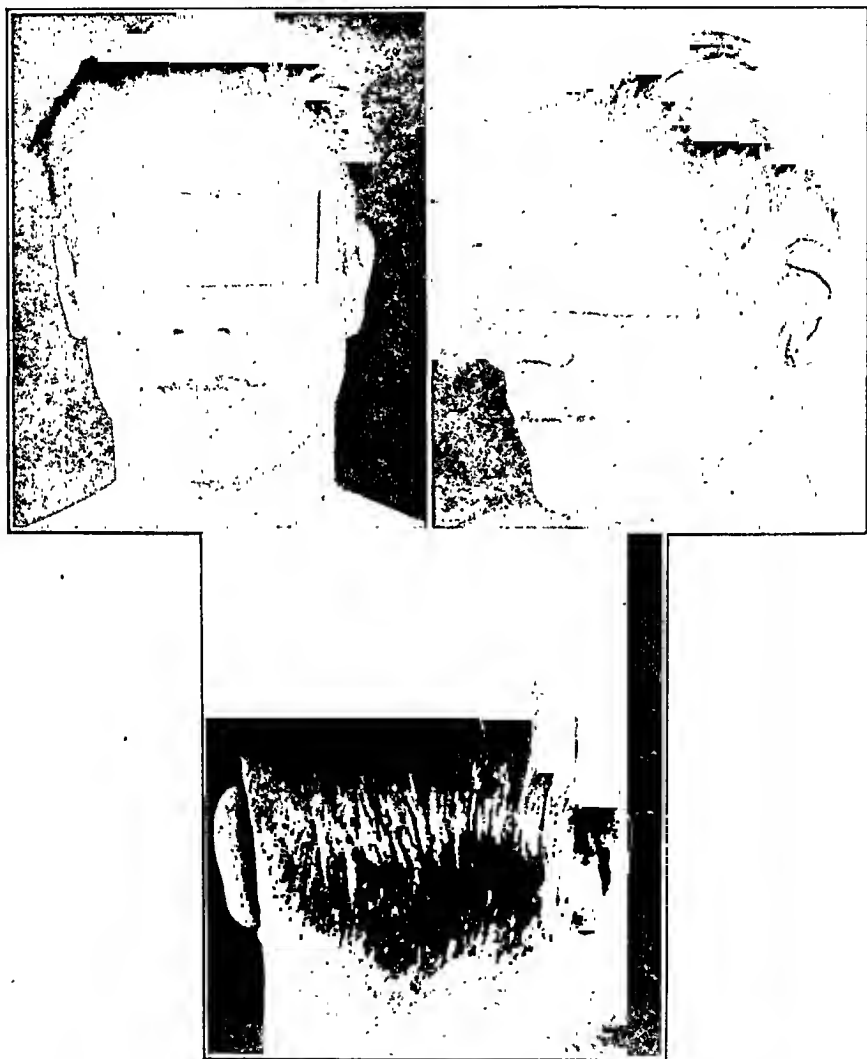


Fig. 7.—Final result, twenty-five months after operation.

In order that the scarred periphery might be replaced with an elastic covering, this particular ear was supplemented with a small tube pedicle flap taken from the neck, as described by Pierce<sup>7</sup> (fig. 6). The present

7. Pierce, G. W.: Reconstruction of the External Ear, *Surg., Gynec. & Obst.* 50:601-605 (March) 1930.

condition is shown in figure 7, twenty-five months following the original implantation of the tantalum frame.

#### COMMENT

It is realized that the newly constructed ear in the patient demonstrated is not architecturally ideal. This is due primarily to the extensive scarring in the skin bed from which the ear was made. Were the same procedure to be duplicated in skin of good vascularity, such as in a congenitally absent ear, a far superior result might be anticipated and the second stage utilized here be eliminated entirely.

However, the most important factor seems to be that an ear has been constructed around a tantalum wire model of a normal auricular cartilage. This tantalum structure has remained under the skin for a total of twenty-five months to date (Dec. 1, 1945), during which eighteen months represents the completion of a new ear. With the apparent successful behavior over a reasonably long period, the method should warrant trial by other plastic surgeons. This patient has been discharged from the Navy, but it is planned to follow his future progress in civil life.

#### SUMMARY

1. The subsequent unsuccessful results with Gillies' method of reconstructive otoplasty are discussed.

2. Reemphasis is made for preservation of the ear cartilage when one is dealing with a complete avulsion of the external ear.

3. A new method of reconstructive otoplasty is described, in which a tantalum wire model of an auricular cartilage has been successful and without reaction for over two years.



## BLOCKING OF THE SPLANCHNIC NERVES AND THE FIRST LUMBAR SYMPATHETIC GANGLION

Technic, Accidents and Clinical Indications

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**A**NALYSIS of the evolution of surgery of the sympathetic system during recent years shows that some operations on this system in certain cases have enjoyed a period of enthusiasm followed by another which was less encouraging. In part, this phenomenon may be due to difficulty in determination of an accurate therapeutic indication in every case. The treatment of several diseases by operation on the sympathetic system is based fundamentally on the physiology and physiopathology of the sympathetic system. This being so wide knowledge of the physiology of the sympathetic innervation and of its relation to the disease or to the automatic disturbance is necessary before one decides on this operation. On the other hand, if it is possible before the operation to determine what result may be obtained by operation on the sympathetic system, this type of operation can attain a high degree of accuracy in its therapeutic indications and thus avoid operative failures. By blocking the sympathetic nerves, one can obtain a temporary interruption of their functions, which represents an important preoperative test in surgical measures on the sympathetic system.

In 1914 Kappis<sup>1</sup> introduced anesthesia of the splanchnic nerves, and in 1923 Læwen<sup>2</sup> demonstrated, by infiltrating procaine hydrochloride around the lower thoracic and upper lumbar white rami, that the sensory fibers carrying the painful sensations of the upper abdominal viscera run into the splanchnic nerves, and he determined also the levels at which these fibers enter the cord. Von Gaza<sup>3</sup> (1924) carried out investigations on the use of procaine hydrochloride to determine the pathways of obscure pain. In 1925 Mandl,<sup>4</sup> by para-

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1. Kappis, M.: Erfahrungen mit Lokalanästhesia bei Bauchoperationen, *Verhandl. d. deutsch. Gesellsch. f. Chir.* **43**:87, 1914.

2. Læwen, A.: Weitere Erfahrungen über paravertebrale Schmerzaufhebung zur Differentialdiagnose von Erkrankungen der Gallenblase, des Magens, der Niere, und des Wurmfortsatzes, *Zentralbl. f. Chir.* **50**:461, 1923.

3. von Gaza, W.: Die Resektion der Paravertebralen Nerven und die isolierte Durchseidung des Ramus communicans, *Arch. f. klin. Chir.* **133**:479, 1924.

4. Mandl, F.: Die Wirkung der paravertebralen Injection bei Angina pectoris, *Arch. f. klin. Chir.* **136**:495, 1925.

vertebral anesthetic block, proved that sensory fibers from the heart run to the cord through the upper five or six thoracic rami. After these investigations, important contributions regarding sympathetic innervation and pain were made by Swetlow<sup>5</sup> (1926), Leriche<sup>6</sup> (1927) and Mixer and White<sup>7</sup> (1929). In 1930 White<sup>8</sup> showed that blocking of the sympathetic nerves with procaine hydrochloride is a useful diagnostic procedure to evaluate the quantitative increase in surface temperature that can be produced by sympathectomy and to determine the effect of sympathectomy on obscure pain referred over the sympathetic system. Since then, investigations have been carried out by Woodbridge<sup>9</sup> (1930), Morton and Scott<sup>10</sup> (1931), De Takats<sup>11</sup> (1931), Flothow<sup>12</sup> (1931), Leriche and Fontaine<sup>13</sup> (1934), Ruth<sup>14</sup> (1934), Leriche<sup>15</sup> (1940), Outland and Hanlon<sup>16</sup> (1940), Sousa Pereira<sup>17</sup> (1941), and Rovenstine and Wertheim<sup>18</sup> (1941) on anesthetic block of the sympathetic pathways as a method of diagnosis, a preoperative test or a method of treatment.

After I recognized the importance of the preoperative study of the innervation of the sympathetic system, I began performing its physiologic interruption as a test to determine the influence of block-

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5. Swetlow, G. I.: Paravertebral Alcohol Block in Cardiac Pain, *Am. Heart J.* **1**:393, 1926.

6. Leriche, R.: *La chirurgie de la douleur et ses resultats*, Presse méd. **35**:497 and 561, 1927.

7. Mixer, W. J., and White, J. C.: Alcohol Injection in Angina Pectoris, *Ann. Surg.* **89**:199, 1929.

8. White, J. C.: Diagnostic Novocain Block of the Sensory and Sympathetic Nerves: A Method of Estimating the Results Which Can Be Obtained by Their Permanent Interruption, *Am. J. Surg.* **9**:264, 1930.

9. Woodbridge, P. D.: Therapeutic Nerve Block with Procaine and Alcohol, *Am. J. Surg.* **9**:278, 1930.

10. Morton, J. J., and Scott, W. J. M.: Methods for Estimating the Degree of Sympathetic Vasoconstriction in Peripheral Vascular Diseases, *New England J. Med.* **204**:955, 1931.

11. de Takats, G.: The Differentiation of Organic and Spastic Vascular Occlusions, *Ann. Surg.* **94**:321, 1931.

12. Flothow, P. G.: Diagnosis and Therapeutic Injections of the Sympathetic Nerves, *Am. J. Surg.* **14**:591, 1931.

13. Leriche, R., and Fontaine, R.: Technic of and Indications for Procaine Hydrochloride Infiltration of Lumbar Sympathetic, *Presse méd.* **42**:1843, 1934.

14. Ruth, H. S.: Diagnostic, Prognostic and Therapeutic Nerve Blocks, *J. A. M. A.* **102**:419 (Feb. 10) 1934.

15. Leriche, R.: *Chirurgie de la douleur*, ed 2, Paris. Masson & Cie, 1940.

16. Outland, T., and Hanlon, C. R.: The Use of Procaine Hydrochloride as a Therapeutic Agent, *J. A. M. A.* **114**:1330 (April 6) 1940.

17. de Sousa Pereira, A.: A technica dos bloqueios anestésicos dos nervos esplanchnicos, *Med. contemp.* **60**: 1941.

18. Rovenstine, E. A., and Wertheim, H. M.: Therapeutic Nerve Block, *J. A. M. A.* **117**:1599 (Nov. 8) 1941.

ing the regional sympathetic system in each patient before operation. These anesthetic blocks were performed singly or were repeated in order to obtain a fairly accurate result. Then, in order to obtain a definitive result, previously ascertained by the physiologic interruption of the sympathetic ganglions or trunks, sympathectomy was performed. After I began following this routine, I observed in my cases an improvement in the results. This effect was especially important in the field of the splanchnic nerves to determine in every case the indications for splanchnicectomy. But in addition to being a preoperative test in this operation, single or repeated anesthetic blocks of the splanchnic nerves may also be a useful method of diagnosis or treatment in certain cases of visceral pain, vasomotor disturbances or disturbances of the tone of the smooth intestinal muscle. The importance of the therapeutic problems related to the splanchnic nerves led me to study these nerves especially. During the last eight years, more than one thousand anesthetic blocks of the splanchnic nerves or of these nerves and the first lumbar sympathetic ganglion have been performed with the technic that will be described. The accidents that have occurred and the indications for operation and the results in the cases that have been studied will also be described.

#### ROUTES OF APPROACH TO ANESTHESIA OF THE SPLANCHNIC NERVES

Kappis<sup>1</sup> was the first to introduce anesthesia of the splanchnic nerves, having made his preliminary report in 1914 to the Congress of Surgery in Berlin. In 1918 he published a report of a series of 200 cases. To reach the nerves he followed a posterior route. This technic will be described later.<sup>19</sup> In the same year Wendling<sup>20</sup> suggested the approach to the splanchnic nerves by the anterior route, by introducing a long needle through the intact anterior abdominal wall a little below and to the left of the ensiform cartilage. This needle, to reach the retroperitoneal nerves and ganglions, must cross the left lobe of the liver and the lesser omentum. It was demonstrated to be an inaccurate and dangerous method and was quickly abandoned. Braun,<sup>21</sup> in 1919, intro-

19. Kappis, M.: (a) Die Anästhesierung des Nervus splanchnicus, Zentralbl. f. Chir. **45**:709, 1918; (b) Sensibilität und lokale Anästhesie in chirurgischen Gebiet der Bauchhöhle mit besonderer Berücksichtigung der Splanchnicus-Anästhesie Beitr. z. klin. Chir. **155**:161, 1919; (c) Zur Technik der Splanchnicusanästhesie, Zentralbl. f. Chir. **47**:98, 1920; (d) Ueber Splanchnicus anaesthesia, Verhandl. d. deutsch. Gesellsch. f. Chir. **44**:275, 1920; (e) Die Technik der Einspritzungen den Nervus splanchnicus, Zentralbl. f. inn. Med. **46**:1097, 1925.

20. Wendling, H.: Ausschaltung der Nervi splanchnici durch Leitungsanästhesie bei Magenoperationen und andern Eingriffen in der oberen Bauchhöhle, Beitr. z. klin. Chir. **110**:517, 1918.

21. Braun, H.: Ein Hilfsinstrument zur Ausführung der Splanchnicusanästhesie, Zentralbl. f. Chir. **48**:1544, 1921.

duced direct anesthesia of the splanchnic nerves and the solar plexus after a previous laparotomy.

In cases in which it is necessary to anesthetize the abdominal viscera, a previous laparotomy having been performed, anesthesia of the splanchnic nerves can be obtained by following Braun's technic. After a supraumbilical median or paramedian laparotomy has been performed, the left lobe of the liver is retracted upward and the stomach pulled carefully downward and to the left. Thus the lesser omentum is exposed, and with the left forefinger through the omentum one tries to palpate the aorta, which is recognized by its pulsation. In its progress toward the spine, the left forefinger pushes the aorta to the left and the vena cava to the right. A fine needle 12 cm. long is introduced through the lesser omentum so that it passes over the pancreas and between the two blood vessels which are held apart by the left forefinger. The needle goes through the retroperitoneal tissue up to the crura of the diaphragm. After first aspirating to make sure that the needle is not in a blood vessel, one proceeds to inject into the loose prevertebral periaortic tissue 100 cc. of 0.5 per cent solution of procaine hydrochloride. To obtain an easier injection, various mechanical devices have been tried. Kirchmayer,<sup>22</sup> Burke<sup>23</sup> and Denman<sup>24</sup> have described conductors and protecting tubes to direct the needle along the finger.

Injection by the posterior route, described by Kappis,<sup>19</sup> was the first to be put into practice. Its superiority is shown by the fact that it permits one to anesthetize the splanchnic nerves by the lumbar route merely by the introduction of a conveniently directed needle. Here is Kappis' description: The patient lies prone, with a pillow under the costal arch to bend the vertebral column. Seven centimeters from the midline and just below the twelfth rib, a needle 12 cm. long is directed so as to form an angle of 30 degrees with the sagittal plane. When the needle reaches the depth of the vertebral body, one slides it tangentially to the border of the vertebra until its tip has lost contact with the bone, which corresponds to an advance of about 1 cm. Then, after one has aspirated with the syringe to see whether the needle has penetrated a blood vessel, 20 to 40 cc. of 1 per cent solution of procaine hydrochloride is injected. To obtain complete anesthesia, one proceeds similarly in relation to the splanchnic nerves on the opposite side. The bilateral anesthetic blocks are repeated, with a similar technic, at the height of the second lumbar vertebra.

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22. Kirchmayer, L.: Eine gedeckte Nadel zur Splanchnicusanästhesie nach H. Braun, *Zentralbl. f. Chir.* **50**:1480, 1923.

23. Burke, J.: A New Instrument in Splanchnic Anesthesia, *J. A. M. A.* **82**:790 (March 8) 1924.

24. Denman, P. R.: A New Instrument in Splanchnic Anesthesia, *J. A. M. A.* **84**:1179 (April 18) 1925.

In 1920 Kappis<sup>19c, d</sup> began to employ only one injection on either side of the vertebral column. The needle is inserted below the twelfth rib, and 20 cc. of the procaine hydrochloride solution is injected; after this, the needle is directed upward and downward, parallel to the vertebral bodies, and 20 cc. of the solution is injected in either direction. Later Kappis advised only one injection on either side but without the upward and downward slant of the needle.

Labat<sup>25</sup> also described a technic of anesthesia of the splanchnic nerves by a posterior route, similar to that of Kappis. He modified the inclination of the needle from an angle of 30 degrees to one of 45 degrees. Roussiel<sup>26</sup> followed also a posterior approach and named this method paravertebral anesthesia.

Two technics of anesthesia of the splanchnic nerves must be kept in mind. In cases in which previous laparotomy has been performed, Braun's technic, by the anterior route, is indicated. The technic of Kappis, by the posterior route, permits injection of anesthetic solution around the splanchnic nerves through a needle introduced just below the last rib and directed toward the anterolateral region of the first lumbar vertebra. This method does not require a previous laparotomy.

De Takats,<sup>27</sup> in 1927, made a complete study of both methods of anesthetizing the splanchnic nerves, anterior and posterior. From the technical point of view, the problem consists in infiltration of the loose connective tissue which lies in front of the first lumbar vertebra with the anesthetic solution, and this can be done by either the anterior or the posterior route. He demonstrated that experimental and clinical facts showed that bilateral anesthetic block of the splanchnic nerves leads to anesthesia of the upper abdominal organs. Comparing the results of anesthesia induced by injections by a posterior approach, obtained in 2,335 cases, with those of anesthesia induced by injections by an anterior route, obtained in 1,222 cases, de Takats concluded that the injection by the anterior route yielded better results and carried less risk than that by the posterior one. It is true that the anterior route permits injection of the anesthetic solution close to the splanchnic nerves and the solar plexus directly and under control of the finger. As it necessitates a previous laparotomy, this technic is indicated in only a

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25. Labat, G.: L'anesthésie splanchnique dans les interventions chirurgicales et dans les affections douloureuses de la cavité abdominale, *Gaz. d. hôp.* **93**:662, 1920; Regional Anesthesia with Special Reference to Splanchnic Analgesia, *Brit. J. Surg.* **8**:278, 1921; The Induction of Splanchnic Analgesia, *Ann. Surg.* **80**:161, 1924; Regional Anesthesia, Philadelphia, W. B. Saunders Company, 1922, p. 350.

26. Roussiel, M.: Anesthésie des nerfs splanchniques et des plexus mésentériques supérieurs et inférieurs en chirurgie abdominal, *Presse méd.* **31**:4, 1923.

27. de Takats, G.: Splanchnic Anaesthesia: A Critical Review of the Theory and Practice of This Method, *Surg., Gynec. & Obst.* **44**:501, 1927.

limited number of cases. In all cases in which it is necessary to perform anesthetic block of the splanchnic nerves without previous laparotomy, only the posterior route is suitable. My colleagues and I have seen that repeated punctures in the same place and at short intervals in order to block the splanchnic nerves by the posterior route quickly become painful and unbearable by the patient. Observation of this fact led me to study a technic that would be better tolerated by patients.

ANATOMIC FACTS ON WHICH IS BASED THE TECHNIC  
OF BLOCK OF THE SPLANCHNIC NERVES BY  
THE POSTERIOR ROUTE

Dissection and study of the splanchnic nerves, the solar plexus and the thoracolumbar sympathetic chain in 100 human cadavers led me to the following conclusions regarding the morphology and topography of these nerves.<sup>28</sup>

The splanchnic nerves establish the connection between the thoracic sympathetic chain and the solar plexus (fig. 1). Normally two splanchnic nerves effect this connection (53 per cent of cases). Less often (43 per cent) there are three splanchnic nerves. In rare cases (4 per cent) there are four splanchnic nerves. These are the greater splanchnic, the lesser splanchnic, the lowest splanchnic and the accessory splanchnic. The greater splanchnic nerve originates in the segment of the thoracic sympathetic chain lying between the fourth and eleventh thoracic ganglion. It is usually formed by three branches or, less often, by four or five. It may also be constituted by as few as one or as many as seven branches. Most frequently the branches of the greater splanchnic nerve come from the seventh, eighth and ninth thoracic sympathetic ganglia. These branches run downward and obliquely inward on the anterolateral aspect of the spine and come together at various levels to form a cord, which in its downward course passes over the anterolateral aspect of the body of the last thoracic vertebra. It perforates the crura of the diaphragm and divides into its terminal branches, ending in the semilunar ganglion. At the origin of the trunk of the greater splanchnic was found in about 70 per cent of cases a small ganglion (splanchnicum ganglion), normally opposite the level of the eleventh or twelfth thoracic vertebrae.

The greater splanchnic nerve pierces the diaphragm usually (63 per cent) through the space which separates the internal from the external crus of the vertebral insertion of the diaphragm. In other cases (13 per cent) this nerve perforates directly the single crus. The internal crus is perforated in 9 per cent of cases and the external crus in 3 per cent, or the nerve passes through the space between the internal and inter-

28. de Sousa Pereira, A.: *Nervi splanchnici*, Thesis, Oporto, Portugal, 1929.

medial crura as verified in 6 per cent of cases. Only rarely (3 per cent) does the greater splanchnic nerve penetrate the abdomen by the aortic hiatus. Whatever the route followed by the greater splanchnic nerve across the diaphragm, after it enters the abdominal cavity it is directed obliquely downward and inward or, at other times, transversely inward and divides into various terminal branches, which spread out like a fan. A great number of these fibers go to the semilunar ganglion, where they terminate; others are directed to the aorticorenal



Fig. 1.—Abdominal and pelvic sympathetic innervation: 1 and 6, adrenal glands; 2, greater splanchnic nerve; 3, adrenal sympathetic fibers coming from the solar plexus; 4, renal plexus; 5, superior hypogastric plexus; 7, solar plexus; 8, aorticorenal ganglion; 9, aortic plexus; 10, lumbar sympathetic chain; 11, inferior hypogastric plexus.

ganglion or to the cord which connects this ganglion with the semilunar ganglion.

The lesser splanchnic nerve is usually formed by two branches—sometimes by one or by three—from the thoracic sympathetic chain, between the tenth and twelfth thoracic ganglions. Soon after their origin these branches converge into one trunk, which descends down-

ward, inward and forward along the lateral aspect of the spine, between the greater splanchnic nerve and the sympathetic chain. When it reaches the diaphragm, the lesser splanchnic nerve usually insinuates itself into the interstice which separates the internal and external crura (68 per cent), under the greater splanchnic nerve and in front of the sympathetic chain. Less often it perforates the single crus (6 per cent), the internal crus (3 per cent) or the external crus (2 per cent) or passes between the internal and intermedial crura (7 per cent). In some cases it enters the abdominal cavity through the aortic hiatus (9 per cent). The lesser splanchnic nerve, after entering the abdomen, normally emerges from the diaphragmatic crura 1 or 2 cm. below the greater splanchnic nerve. From its point of entry into the abdominal cavity to its ending in the aorticorenal ganglion or the semilunar ganglion, to pass to the renal plexus the lesser splanchnic nerve generally follows an obliquely downward course, sometimes a transverse one and rarely a recurrent course.

The lowest splanchnic nerve, observed in 43 per cent of cases, is usually made up of a single branch or, rarely, of two branches which originate from the ganglions or from the intermediary cord of the sympathetic system, between the tenth and twelfth thoracic ganglions. This nerve, which is usually an extremely fine cord situated behind and below the lesser splanchnic nerve and in front of the sympathetic chain, follows a nearly rectilineal course from its origin to the diaphragm between these two nerves or between the lesser splanchnic nerve and the accessory splanchnic nerve when it exists. It normally enters the abdomen by the space between the internal and external crura of the diaphragm, below the greater and the lesser splanchnic nerves and above the lumbar sympathetic chain. Only rarely does it perforate the single crus, the internal crus or the external crus or pass through the aortic hiatus. In the abdominal cavity the lowest splanchnic nerve extends toward the origin of the renal artery and almost always terminates in the aorticorenal ganglion.

The accessory splanchnic nerve, which I have found 4 times in 100 cases, is a fine cord, independent of the lowest splanchnic nerve but with a similar course. Originating from the eleventh or the twelfth thoracic ganglion, it descends alongside the lowest splanchnic nerve, with similar anatomic relations, and ends in the aorticorenal ganglion.

The splanchnic nerves normally terminate at the external border of the solar plexus, which is formed by a series of different-sized ganglions anastomosed among themselves by numerous cords (fig. 1). The solar plexus, a network of ganglions in which some authors describe three groups of symmetric ganglionic masses (semilunar, superior mesenteric and aorticorenal ganglions), presents a variable disposition, not fitting into any rigid pattern. In my dissections I found that the



nerve ganglions and the cords that connect them usually form a flat, more or less tightly meshed network, extending transversely in front of the aorta and surrounding the celiac artery and the root of the superior mesenteric artery. In the transverse plane the solar plexus occupies the space between the two adrenal glands, passes beyond the lateral borders of the aorta on both sides and rests in front of the crura of the diaphragm and the commencement of the abdominal aorta (fig. 1). The greater splanchnic nerve, after crossing the crura of the diaphragm, ends in the upper pole of the lateral border of the solar plexus. In many cases, at this level there exists a ganglion mass which is more voluminous than the neighboring ganglions and which is generally called the semilunar ganglion. The lesser splanchnic nerve, the lowest splanchnic nerve and the accessory splanchnic nerve terminate at the external border of the solar plexus, at points which vary from case to case but which lie in a region situated between the semilunar and aorticorenal ganglions.

The solar plexus occupies an area 2 or 3 cm. high by 3 or 4 cm. wide between the origin of the celiac artery and that of the renal arteries. From it emerge secondary plexuses, which accompany the celiac artery (celiac plexus), the superior mesenteric artery (superior mesenteric plexus), the phrenic arteries, (phrenic plexus), the suprarenal arteries (suprarenal plexus) and the renal arteries (renal plexus). Normally situated in front of the first lumbar vertebra, the upper border of the solar plexus in some cases extends on to the inferior portion of the last thoracic vertebra, and in some cases the lower portion of the plexus corresponds to the second lumbar vertebra. In relation to the soft parts, the upper limit corresponds to the aortic hiatus of the diaphragm and the lower limit corresponds to the origin of the renal arteries. Situated in front of the aorta and the crura of the diaphragm, above the pancreas and within the internal borders of the suprarenal glands, the solar plexus covered in front by the peritoneum, lies in a connective tissue, rich in fat, in which there are lymphatic ganglions and numerous lymph and blood vessels. Caudalward the solar plexus is continuous with the aortic plexus, from which arises part of the spermatic, the inferior mesenteric and the hypogastric plexuses (fig. 1). It is known at the present time that the splanchnic nerves carry the sensory fibers for a large group of abdominal organs. Anesthetic block of the splanchnic nerves results in anesthesia of the organs innervated by these nerves.

#### MORPHOLOGY AND TOPOGRAPHY OF THE TWELFTH RIB: ITS RELATION TO THE POSTERIOR ROUTE OF ANESTHETIC BLOCK

According to the technic of anesthesia of the splanchnic nerves induced by the posterior route, described by Kappis, the needle must be

inserted 7 cm. from the midline, just below the inferior border of the twelfth rib, and must be directed in such a way that it permits injection of the anesthetic solution close to the splanchnic nerves and the solar plexus. If the morphology of the last rib were always the same and if the angle formed by this rib with the medium plane were invariable, the reference point established by Kappis should be accurate. Such, however, is not the case. On the contrary, it is known that the solar plexus and the terminal portion of the splanchnic



Fig. 2.—Topography of the splanchnic nerves and solar plexus in relation to the skeleton.

nerves generally correspond to the first lumbar vertebra (fig. 2), and the renal arteries are found normally at the level of the second lumbar vertebra. The anesthetic solution should be injected above these vessels, in particular at the level of the first lumbar vertebra.

The point of the lower border of the twelfth rib, which is 7 cm. from the midline, differs with the angle of inclination of the last rib. This angle varies within wide limits (fig. 3) not only from case to case but from the right side to the left side in the same person (see the

table). In twenty roentgenograms of the thoracolumbar portion of the spine and the twelfth rib, I have studied the angle formed by the last rib with the lumbar portion of the spine and also the total length of this rib. The results are given in the table. Thus I have demonstrated that the angle formed by the inferior border of the twelfth rib and the lumbar portion of the spine varies from 30 to 70 degrees. The angles most frequently found were between 40 and 55

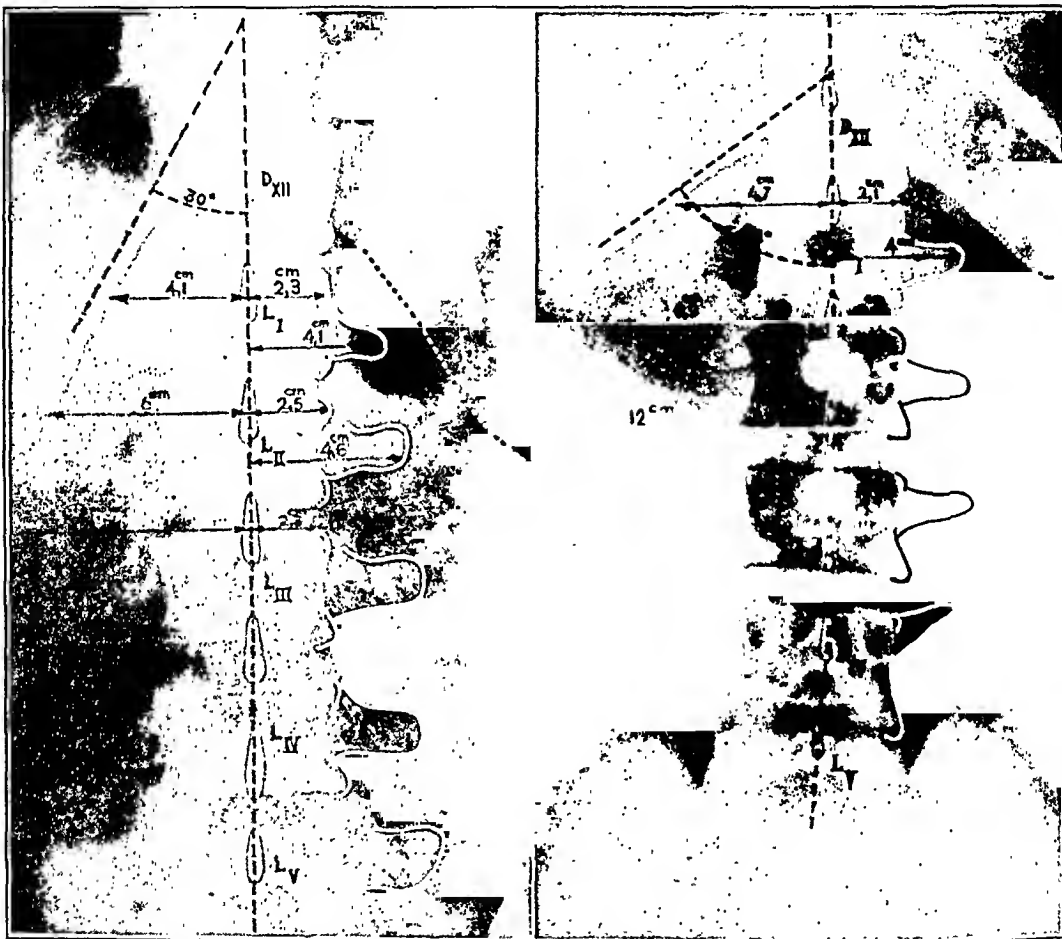


Fig. 3.—Roentgenograms and diagrams which show the difference in the angle of incidence of the lower border of the twelfth rib in relation to the axis of the spine. Note also the width of the vertebral bodies and the length of the transverse processes in relation to the midline.

degrees. These observations showed that in the majority of cases a horizontal line traced through a point situated 7 cm. from the midline in the lower border of the last rib corresponds to the second lumbar vertebra. Only in rare cases was it situated in front of the first lumbar vertebra. It also must be remembered that the length

of the twelfth rib is variable (fig. 4). In the 20 cases studied, the twelfth rib had lengths ranging from 3 to 15 cm. On the right side ribs 10 cm. long were found, and on the left side the length varied from 6 to 13 cm. This being so, not only must the angle of the twelfth rib be previously determined by palpation or roentgenologic examination but also accurate information on the length of the last rib must be obtained.

#### AREA WHERE BLOCK OF THE SPANCHNIC NERVES IS PRACTICED

Several technics have been described (Kappis<sup>19</sup> and Labat<sup>25</sup>) for block of the splanchnic nerves with anesthetic infiltration by the pos-

#### *Measurements of Twelfth Rib as Taken from Twenty Roentgenograms*

| Number of Cases | Angle Formed by the Right 12th Rib, Degrees | Angle Formed by the Left 12th Rib, Degrees | Length of the Right 12th Rib, Cm. | Length of the Left 12th Rib, Cm. |
|-----------------|---|--|-----------------------------------|----------------------------------|
| 1.....          | 35  | 33   | 15                                | 13                               |
| 2.....          | 60  | 40   | 5                                 | 10                               |
| 3.....          | 55  | 40   | 12                                | 11                               |
| 4.....          | 50  | 55   | 4                                 | 6                                |
| 5.....          | 35  | 45   | 9                                 | 9.5                              |
| 6.....          | 55  | 50   | 10                                | 9                                |
| 7.....          | 55  | 35   | 10                                | 9.5                              |
| 8.....          | 55  | 60   | 10                                | 10.5                             |
| 9.....          | 40  | 45   | 5.5                               | 3                                |
| 10.....         | 40  | 45   | 12                                | 10                               |
| 11.....         | 60  | 55   | 4.5                               | 5                                |
| 12.....         | 40  | 45   | 12.5                              | 11.5                             |
| 13.....         | 45  | 55   | 8                                 | 7                                |
| 14.....         | 50  | 45   | 10                                | 12                               |
| 15.....         | 70  | 65   | 10                                | 9                                |
| 16.....         | 45  | 45   | 11.5                              | 7                                |
| 17.....         | 55  | 35   | 10                                | 12                               |
| 18.....         | 50  | 40   | 11                                | 13                               |
| 19.....         | 54  | 48   | 8                                 | 6                                |
| 20.....         | 30  | 42   | 14                                | 11.5                             |

terior route. When these technics are followed, the needle is introduced into a preestablished point, located 7 cm. from the midline, just below the lower border of the twelfth rib. However, study of the morphology and topography of the splanchnic nerves in relation to the last rib showed that variations exist from case to case. Also in patients on whom I have employed these technics I have observed that punctures in the same place and repeated at short intervals are painful and badly tolerated. These two facts led me to try to develop a technic that would permit one to perform repeated, even daily, anesthetic blocks of the splanchnic nerves and sympathetic chain, without the procedures becoming unbearable. I tried to determine not a point, as Kappis did, but an area in which it was possible to introduce a needle, always at

different points, and to direct it so that the terminal portion of the splanchnic nerves was infiltrated by the anesthetic solution.

From my investigations I have concluded that the best area is represented by a triangle (fig. 5) which is bounded internally by the body of the first lumbar vertebra and by the upper half of the body of the second lumbar vertebra, above by the lower border of the twelfth rib and below by a transverse plane passing midway between the spinous processes of the first and second lumbar vertebra. The terminal portion of the splanchnic nerves and the external border of the solar plexus correspond in depth to the internal side of this triangle (fig. 6).

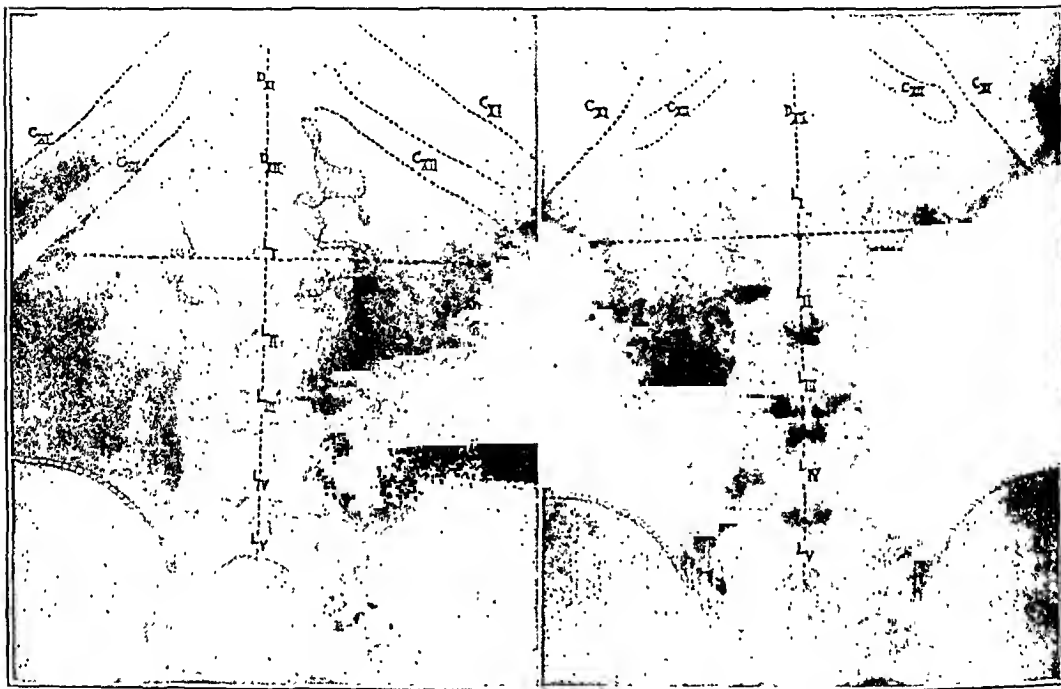


Fig. 4.—A, morphology of the twelfth rib and triangle formed by the transverse plane passing at the level of the transverse processes of the second lumbar vertebra. B, morphology of the twelfth rib and triangle formed by the transverse plane passing at the level of the transverse processes of the second lumbar vertebra.

#### TECHNIC OF ANESTHETIC BLOCK OF THE SPLANCHNIC NERVES AND THE FIRST LUMBAR GANGLION

After previous determination of the arterial blood pressure, the patient is placed in a sitting position, with the dorsolumbar region exposed. He flexes his trunk and rests the hands on his thighs or on the edge of the bed (fig. 7). If his condition does not permit this position, he is placed in the lateral decubitus position, back arched and knees flexed. By inspection, palpation or roentgenologic examination, an exact idea of the topography of the last rib and of the spinous proc-

esses of the first and second lumbar vertebrae is acquired. A transverse plane midway between these two processes and passing laterally until the lower border of the twelfth rib is reached is drawn. This plane normally corresponds to the transverse process of the second lumbar vertebra. Within the triangle bounded inferiorly by this plane, above by the lower border of the twelfth rib and internally by the lateral aspect of the body of the first and second lumbar vertebrae, an



Fig. 5.—Triangle in which the punctures for splanchnic nerve block should be done. This triangle is bounded internally by the external border of the first and second lumbar vertebrae, above by the lower border of the last rib and below by a transverse plane passing halfway between the spinous processes of the first and second lumbar vertebrae. In depth this plane corresponds to the transverse processes of the second lumbar vertebra.

area remains in which it is possible to insert a needle that will carry the anesthetic close to the splanchnic nerves (fig. 7).

The inner limits for the insertion of the needle is 2.5 cm. from the midline. If the needle is introduced at this distance it must be directed parallel to the sagittal plane and pass above or below the transverse

process of the first lumbar vertebra (figs. 8 and 9). Once the needle has passed at a tangent to the body of the vertebra, it is advanced 1 to 2 cm. farther. At this point it is felt that the needle, after piercing the muscular aponeurotic plane, enters in a free space. Its tip is then in the loose connective tissue which surrounds the terminal portion of the splanchnic nerves and the external border of the solar plexus. Aspiration is made with the syringe to make sure that the needle has not penetrated a blood vessel. Then 30 to 35 cc. of a 1 per cent anesthetic



Fig. 6.—Deep topography of the triangle (fig. 5) in the area of which must be inserted the needle to produce the anesthetic block of the splanchnic nerves and first lumbar sympathetic ganglion: 1, solar plexus; 2, greater splanchnic nerve; 3, lesser splanchnic nerve; 4, lumbar sympathetic chain; 5, sacralis sympathetic chain; 6, adrenal gland; 7, semilunar ganglion; 8, renal plexus; 9, superior hypogastric plexus.

solution of procaine hydrochloride is injected slowly, so as to avoid the sudden dissociation of the tissues that may cause some rupture of small vessels and give rise to a hematoma. Several times during the injection, aspiration is done to make sure that the needle is not in a vessel. The other points at which the needle may be introduced are

situated within the area of the aforementioned triangle (fig. 7), between its internal border and the lower border of the last rib. When this rib is approached, it is necessary to increase progressively the angle of inclination of the needle in relation to the sagittal plane so that the needle passes deeply at a tangent to the body of the vertebra (figs. 8 and 9). The needle is made to progress 1 to 2 cm., and in the same way, once the musculoaponeurotic plane is passed, the point of the needle gives the sensation of less resistance, which shows that it has reached the loose connective tissue in which the splanchnic nerves are located.

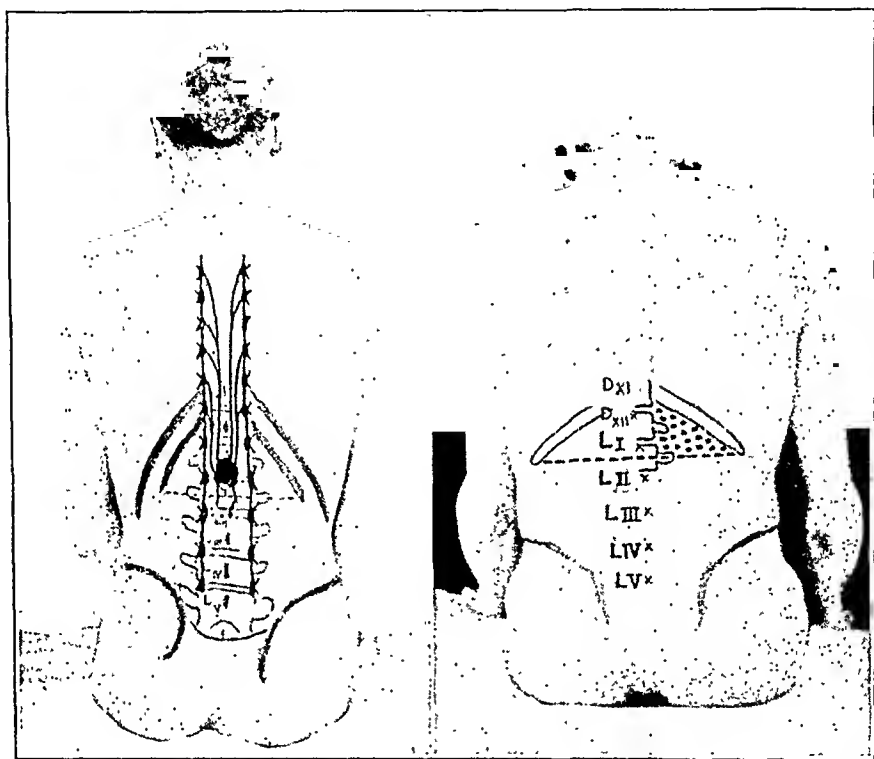


Fig. 7.—Demarcation of the triangle within which the needle must be inserted to perform the anesthetic block of the splanchnic nerves. Topography of the splanchnic nerves in relation to the skeleton and sitting position of the patient for the anesthetic block.

To block especially the first lumbar sympathetic ganglion and the splanchnic nerves by the same approach (fig. 10), the needle is inserted in the area of the triangle above the transverse process of the first lumbar vertebra. From 2.5 cm. of the midline to the lower border of the twelfth rib the needle may be introduced in any place within the area of the triangle (fig. 7). The needle is inserted parallel to the sagittal plane or obliquely, according to the place of puncture. It must be directed in order to pass deeply tangential to the body of the



first lumbar vertebra. After the needle is so directed, it is introduced about 1 cm. more and one begins injecting 3 to 5 cc. of the anesthetic solution into the musculoaponeurotic tissue at the same time that the needle is slowly introduced until one feels that its point is free and that the anesthetic solution diffuses quickly and easily into the prevertebral loose connective tissue. When the point of the needle attains this plane in front of the body of the vertebra, 5 cc. more of the anesthetic solution is injected in this plane. This anesthetic solution blocks the



Fig. 8.—The two sections shown in figure 9 were done, one, *A*, 0.5 cm. above the transverse processes of the first lumbar space and the other, *B*, at the level of the transverse processes of the second lumbar space.

sympathetic chain at the level of the first lumbar ganglion that is placed against the body of the first lumbar vertebra. The needle is then introduced 1 to 2 cm. farther into the loose connective tissue that surrounds the terminal portion of the splanchnic nerves. Into this tissue 25 cc. of 1 per cent solution of procaine hydrochloride is injected. If the needle is inserted below the transverse process of the first lumbar vertebra in the area of the same triangle (fig. 7), it must be directed

upward in order to reach the first lumbar ganglion and the splanchnic nerves in front of the first lumbar vertebra.

After one gains experience with the technics described, the needle may be quickly introduced near the body of the vertebra, without touching the periosteum. It is important to avoid punctures of the bone,

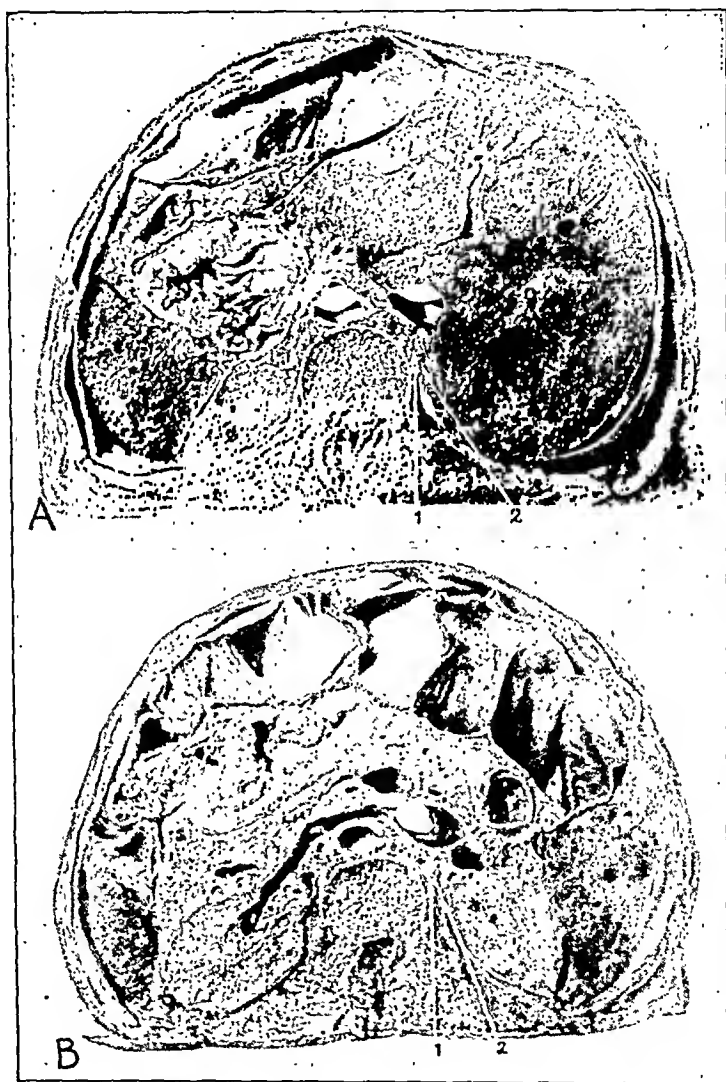


Fig. 9.—Directions which should be given to the needle (1 and 2) according to the point of puncture so as to reach the abdominal segment of the splanchnic nerves. *A*, transverse section passing 0.5 cm. above the superior border of the transverse processes of the first lumbar space. *B*, section at the level of the transverse processes of the first lumbar space and catching the renal pedicle.

because they are painful. When repeated anesthetic blocks of the splanchnic nerves are necessary, it is possible to change the point of insertion of the needle in the area of the triangle (fig. 5). Repeated

punctures, always at different points, are easily tolerated by the patient. Using the technic described, I have performed repeated anesthetic blocks of the splanchnic nerves alone or of these nerves and the first lumbar ganglion. The results were controlled by study of the arterial blood pressure and the degree of glycemia. The increase in temperature and the changes in cutaneous resistance at the level of

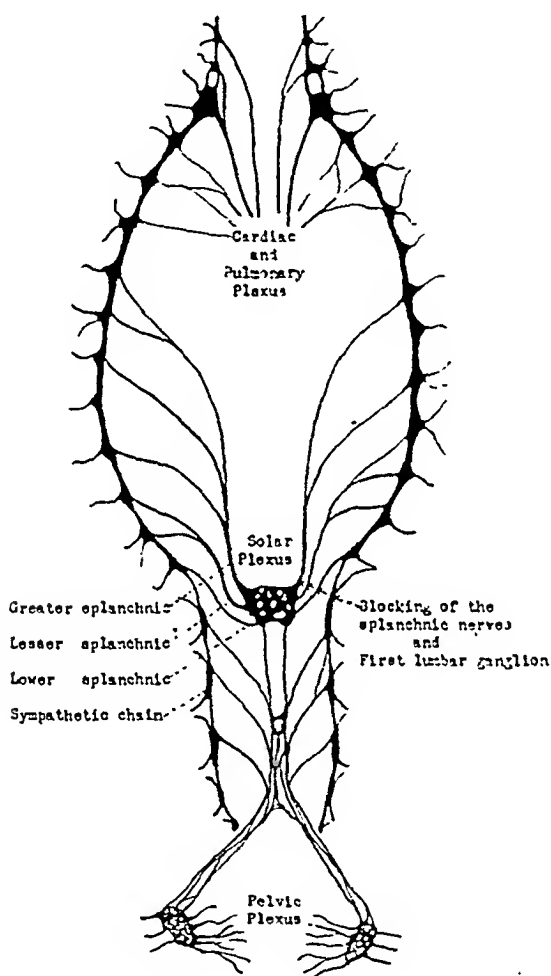


Fig. 10.—Block of the first lumbar sympathetic ganglion and the splanchnic nerves by the same approach.

the lower extremity showed the result of the anesthetic block of the first lumbar ganglion of the sympathetic chain. The results that I have obtained in a large series of cases using that technic justify the description of the technic. For my co-workers and myself, this technic was normally followed by successful results and was well tolerated by the patients.

ACCIDENTS WHICH MAY OCCUR IN THE COURSE OF BLOCK-  
ING THE SPANCHNIC NERVES AND THE FIRST  
LUMBAR SYMPATHETIC GANGLION

Normally, anesthetic block of the splanchnic nerves or of these nerves and the first lumbar sympathetic ganglion is well tolerated by patients. Some patients, however, especially those that have low arterial blood pressure, may feel after the injection of the anesthetic solution a temporary and slight sensation of dizziness or faintness, sometimes accompanied with a subjective visual disturbance. These sensations are probably caused by cerebral ischemia at the same time that the blood pressure becomes lower. This ischemia is probably due to visceral vasodilatation in the field of the innervation of the splanchnic nerves blocked by the anesthetic solution. To avoid these disturbances, which may appear a few minutes after anesthetic block of the splanchnic nerves, the patient is always placed in the dorsal decubitus, with head low. The sensations disappear completely, without damage to the patient, one hour or less after the anesthetic injection.

During the block of the splanchnic nerves, the tip of the needle may sometimes perforate a deep vessel and blood may appear in the hub of the needle. It is important to avoid injection of the anesthetic solution into a vessel. To be sure that the injection is not intravascular, it is necessary to aspirate with the syringe before the injection is made and during the injection if the direction of the needle changed with the maneuvers of the injection. In a few instances, I have observed that when the needle was introduced to block the left splanchnic nerves the patient sometimes felt pain at the level of the heart. This pain disappeared after the injection of the anesthetic solution. Investigations that I have carried out on patients on whom I have performed splanchnicectomy while they were under local anesthesia showed that mechanical stimulation of the left splanchnic nerves may produce pain at the level of the heart. Anesthesia of these nerves during the mechanical stimulation immediately abolished the precordial pain. These facts led me to believe that pain at the level of the heart produced by the introduction of the needle to reach the left splanchnic nerves is probably caused by the stimulation of the left splanchnic nerves.

During a period of eight years of investigation with single or repeated anesthetic blocks of the splanchnic nerves, I have observed only one serious complication, in a patient with gastric ulcer who was being treated by repeated anesthetic blocks of the splanchnic nerves. Once, when the needle was introduced into the left side and when the injection of the anesthetic solution started, the patient immediately had a convulsion, lost consciousness and stopped breathing. Oxygen was administered, and respiration was restored by artificial means. A few minutes later the patient began to breathe, and twenty minutes

later he became conscious. It was then seen that the right upper and lower extremities were paralyzed. Twenty-four hours later paralysis had not improved. In attempting to interpret this accident, which I had never seen before, I began to think that it was probably the result of a cerebral vascular spasm, caused by the mechanical stimulation of the left splanchnic nerves. In accordance with this hypothesis, I performed an anesthetic block of the left middle and stellate ganglions, which was followed by a favorable influence on the paralysis of the extremities. Two days later another block of the same ganglions was performed. One week after the accident, the patient had recovered and the paralysis of the extremities of the right side had disappeared.

During my studies in this field, with more than one thousand anesthetic blocks of the splanchnic nerves, I never saw a repetition of this accident. The favorable influence of the anesthetic block of the middle cervical and stellate ganglions and the disappearance of the paralysis suggest that in this case the mechanism of the paralysis was probably a reflex spasm of the vessels of the brain caused by the mechanical stimulation of the left splanchnic nerves.

#### CLINICAL INDICATIONS

The clinical problems related to the splanchnic nerves have been investigated more intensively in the last years than formerly and have particularly interested the surgeons. The results already obtained are encouraging. In a complex field such as the splanchnic nerves and the solar plexus, one must proceed with caution to find the right procedure and to learn to interpret the results of clinical effects through action on these nerves. From the studies carried on up to this time, it is deduced that the single or the repeated anesthetic block of the splanchnic nerves seems to be a useful method by which to study the effects of temporary interruption of the splanchnic nerves alone or associated with the sympathetic chain at the level of the first lumbar ganglion.

*I. Anesthetic Block of the Splanchnic Nerves.*—1. In Cardiospasm: The cardia is innervated by the vagus and sympathetic nerves. Motor control of the cardia and lower part of the esophagus is effected by local automatism and reflexes through Auerbach's plexus and by long reflexes through the vagi efferents and through the splanchnic efferents (Carlson, Boyd and Percy<sup>29</sup>). Carlson<sup>30</sup> observed in the cat that the splanchnic nerves, like the vagi, contain both motor and inhibitory

29. Carlson, A. J.; Boyd, T. E., and Percy, J. F.: Studies on the Visceral Sensory Nervous System: XIV. The Reflex Control of the Cardia and Lower Esophagus, *Arch. Int. Med.* **30**:409 (Oct.) 1922.

30. Carlson, A. J.; Boyd, T. E., and Percy, J. F.: Studies in the Visceral Sensory Nervous System: XIII. The Innervation of the Cardia and the Lower End of the Esophagus in Mammals, *Am. J. Physiol.* **61**:14, 1922.

efferent fibers to the cardia and lower part of the esophagus. Carlson and co-workers<sup>29</sup> demonstrated in the cat and dog that the inhibition reflex seems to be evoked more readily through the vagal efferent and the motor reflex through the splanchnic efferent fibers. Cardiac reflexes initiated by the splanchnic afferent fibers are predominantly motor.

According to Hurst and Rake,<sup>31</sup> four abnormal conditions may affect the nervous control of the cardiac sphincter: vagus hyperactivity or hypoactivity and sympathetic hyperactivity or hypoactivity. Absence of vagus impulses, resulting in achalasia of the cardia and overaction of the sympathetic impulses producing cardiospasm, are the two factors that probably play the most important part in dysfunction of the cardiac sphincter. Cardiospasm may occur as a reflex result of acute inflammation or carcinoma of the lower portion of the esophagus, peptic ulcer and possibly duodenal ulcer or gallbladder disease (Kuntz<sup>32</sup>). In spasm of the cardiac sphincter, Pottenger<sup>33</sup> pointed out the presence of sympathetic reflexes. In the production of these reflexes, both afferent and efferent impulses course over the sympathetic system.

The conception of treatment of cardiospasm through action on the sympathetic innervation was tested in patients after it was demonstrated that in the bilaterally vagotomized cat (Knight<sup>34</sup>) or monkey (Ferguson<sup>35</sup>) the presence of cardiospasm can be relieved by section of the sympathetic nerves that supply the sphincter. In 2 cases of achalasia with cardiospasm and in 1 case of hypertrophic stenosis of the cardia, Knight<sup>36</sup> performed resection of the left gastric artery with its surrounding nerves that supply the cardiac sphincter. The first 2 patients were improved by sympathectomy, but the third patient was not completely relieved. Meade<sup>37</sup> reported 1 case of sympathectomy, and Ochsner and DeBakey<sup>38</sup> reviewed the literature and collected 19 cases of achalasia in which sympathectomy was done. There was 1 death;

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31. Hurst, A. F., and Rake, G. W.: Achalasia of the Cardia, *Quart. J. Med.* **23**:491, 1930.

32. Kuntz, A.: *Autonomic Nervous System*, ed. 2, Philadelphia, Lea & Febiger, 1934, p. 530.

33. Pottenger, F. M.: *Symptoms of Visceral Disease*, St. Louis, C. V. Mosby Company, 1944, p. 253.

34. Knight, G. C.: The Relation of the Extrinsic Nerves to the Functional Activity of the Esophagus, *Brit. J. Surg.* **22**:155, 1934.

35. Ferguson, J. H.: Effects of Vagotomy on the Gastric Functions of Monkeys, *Surg., Gynec. & Obst.* **62**:689, 1936.

36. Knight, G. C.: Sympathectomy in the Treatment of Achalasia of the Cardia, *Brit. J. Surg.* **22**:864, 1935.

37. Meade, H. S.: A Case of Sympathectomy in the Treatment of Achalasia of the Cardia, *Irish J. M. Sc.*, 1939, p. 130.

38. Ochsner, A., and DeBakey, M.: Surgical Considerations of Achalasia: Review of the Literature and Report of Three Cases, *Arch. Surg.* **41**:1146 (Nov.) 1940.

recurrence took place in 4 cases, and improvement was only partial in 4 patients. In a patient with cardiospasm and pain, Craig, Moersch and Vinson<sup>39</sup> performed bilateral resection of the cervicothoracic sympathetic trunk and ganglions. After the operation the patient was completely relieved of dysphagia and of pain, and she has had no further paroxysmal attacks of the acute type of pain. White and Smithwick<sup>40</sup> pointed out that the results on the whole are not impressive and that further experience is essential. Since previous investigations had put in evidence the probable role of the sympathetic system in the mechanism of cardiospasm, I have tried to analyze its influence through interruption of the splanchnic nerves by anesthetic block. Some facts were observed that can help in the study of the role of sympathetic innervation in cardiospasm.

The first patient to be treated for cardiospasm had also clinical and radiologic signs of megaesophagus and duodenal ulcer. During two weeks, six anesthetic blocks of the right and left splanchnic nerves were performed and the cardiospasm disappeared. Ten more anesthetic blocks were carried out, and one and a half months after the beginning of this treatment the clinical signs of duodenal ulcer and cardiospasm were completely absent. Three years after this treatment the patient remained in good condition. During this period there was no return of duodenal ulcer or cardiospasm.

In a young patient with cardiospasm and megaesophagus, without evident lesions of the stomach or esophagus, repeated anesthetic blocks of the left splanchnic nerves were performed. Five anesthetic blocks in two weeks completely relieved the cardiospasm. For eight months he remained in good condition, but after this period a new crisis of cardiospasm appeared. A new series of eight anesthetic blocks of the left splanchnic nerves was performed, and the cardiospasm was relieved for the second time. At the present time this patient is under observation to see if a new crisis of cardiospasm appears.

A third patient with cardiospasm and megaesophagus was studied. Four weeks after the beginning of his esophagic disturbance there was a narrowing at the level of the cardia that allowed only the passage of fluids. In this patient four anesthetic blocks of the left splanchnic nerves, performed in two days, were not followed by any change in the permeability of the cardia. This patient died of pneumonia two weeks later. Anatomic study of the cardia showed a narrow stenosis caused by scar tissue probably due to healed cardiac ulcer.

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39. Craig, W. M.; Moersch, H. J., and Vinson, P. P.: Treatment of Intractable Cardiospasm by Bilateral Cervicothoracic Sympathetic Ganglionectomy: Report of a Case, *Proc. Staff Meet., Mayo Clin.* 9:749, 1934.

40. White, J. C., and Smithwick, R. H.: *Autonomic Nervous System*, New York, The Macmillan Company, 1944, p. 356.

In a patient with inoperable cancer of the lower portion of the esophagus there was cardiospasm associated with the cancer. Three anesthetic blocks of the left splanchnic nerves brought relief from the cardiospasm during the days of treatment. After splanchnicectomy on the left side was performed, the patient remained improved of her cardiospasm for about one month and then died of internal hemorrhage.

The facts observed in the cases of these patients suggest that repeated anesthetic blocks of the left splanchnic nerves may be useful for relief of cardiospasm, at least in certain cases, also as a method of differential diagnosis between cardiospasm and organic stenosis and as a preoperative test before splanchnicectomy.

2. In Visceral Pain: At the present time it is known that afferent impulses from internal viscera innervated by sympathetic fibers run centrally by afferent spinal neurons which accompany the sympathetic visceral nerves (Pottenger<sup>33</sup>). The visceral afferent pathways enter the spinal cord in the posterior roots, and their axons run to the peripheral plexuses in the visceral nerves. The splanchnic nerves carry the afferent sensory pathways that innervate the stomach, small intestine, liver, gall-bladder and cystic biliary ducts (Davis, Hart and Crain<sup>41</sup>). In pain of the stomach, Head<sup>42</sup> and L  wen have demonstrated that the sensory afferent pathways enter the spinal cord in the sixth, seventh, eighth and ninth thoracic segments. According to Gubergritz and Istschenko,<sup>43</sup> the painful afferent impulses from the kidneys are conducted through the renal plexus and reach the spinal cord through the splanchnic nerves. Investigations made on patients have confirmed the presence of afferent sensory pathways in the splanchnic nerves conducting painful sensations. Mechanical stimulation of the splanchnic nerves performed in patients by Adson<sup>44</sup> and Leriche<sup>45</sup> provoked pain that was relieved by anesthetic block of the splanchnic nerves. Bentley and Smithwick<sup>46</sup> observed that epigastric pain produced by insufflation of a balloon at a certain pressure in the upper jejunum disappeared to the

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41. Davis, L.; Hart, J. T., and Crain, R. C.: The Pathways for Visceral Afferent Impulses Within the Spinal Cord: Experimental Dilatation of the Biliary Ducts, *Surg., Gynec. & Obst.* **48**:647, 1929.

42. Head, H.: On Disturbances of Sensation with Special Reference to the Pain of Visceral Disease, *Brain* **16**:1, 1893.

43. Gubergritz, M. M., and Istschenko, I. N.: Zur Frage der Entstehung der Schmerzempfindungen in den Nieren, *Ztschr. f. d. ges. exper. Med.* **52**:619, 1926.

44. Adson, A. W.: Splanchnic Pain, *Proc. Staff Meet., Mayo Clin.* **10**:623, 1935.

45. Leriche, R.: Des douleurs provoqu  es par l'excitation du bout central des grands splanchniques (douleurs cardiaques, douleurs pulmonaires) au cours des splanchnicotomies, *Presse m  d.* **45**:971, 1937.

46. Bentley, F. H., and Smithwick, R. H.: Visceral Pain Produced by Balloon Distention of the Jejunum, *Lancet* **2**:389, 1940.



right of the midline after the performance of splanchnicectomy on the right side and lumbar sympathectomy. The same degree of distention was not felt after bilateral splanchnicectomy. Low abdominal pain from the lower part of the intestinal tract was relieved in a patient by splanchnicectomy on the right side and resection of the upper lumbar sympathetic ganglions (White and Smithwick<sup>49</sup>). In patients with chronic biliary pain that was intractable to surgical operation, splanchnicectomy was tried, with successful results (Craig<sup>47</sup> and White and Smithwick<sup>49</sup>). From these facts, it is deduced that the fibers carrying painful sensations from the organs innervated by the solar plexus pass through the splanchnic nerves to reach the spinal cord. On the other hand, up to this time it had not been demonstrated that sensory fibers carrying painful sensations from the viscera innervated by the solar plexus pass through the vagus nerves. Then, if the splanchnic nerves are interrupted temporarily by anesthetic block or definitively by splanchnicectomy, visceral pain is relieved in the area innervated by the sensory fibers of these nerves. Knowing this fact, I have been employing anesthetic block as a method of diagnosis or of treatment and as a preoperative test in the indication of splanchnicectomy to relieve visceral pain. As a method of diagnosis, it has been useful to differentiate deep visceral pain from the parietal pain originating at the level of the abdominal wall as it is seen in parietal pain caused by epigastric hernia or in other types of parietal pain. The information obtained by anesthetic block of the splanchnic nerves may be controlled by infiltration with an anesthetic solution of the area of the abdominal wall whence arises the painful stimulation. Anesthetic block of the splanchnic nerves was also important to determine in every case the topography of the sensory fibers that carry the painful visceral sensations.

In cases of inoperable cancer of the stomach accompanied with pain,<sup>48</sup> I have observed that repeated anesthetic blocks of the splanchnic nerves were followed by relief of visceral pain only during one to one and a half hours. However, in a few cases I have observed that anesthetic blocks were followed by relief from pain during a period varying from two hours to few days. In the cases in which relief of pain corresponds only to the time of anesthesia of the splanchnic nerves, there is probably stimulation of the sympathetic innervation by the neoplastic tissue. In the cases in which anesthetic block was followed by relief of pain during several hours or days, the physiologic interruption probably exerts its influence by relieving the vascular spasm that may be a cause of the

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47. Craig, W. M.: Surgical Approach to and Resection of the Splanchnic Nerves for Relief of Hypertension and Abdominal Pain, *West. J. Surg.* **42**:146, 1934.

48. de Sousa Pereira, A.: A cirurgia simpática no tratamento das algias dos cânceros inoperáveis do estômago, *Med. contemp.* **60**:80, 1941.

visceral pain. In the surgical treatment of pain in inoperable cancer of the stomach and the pancreas, I have employed routinely the anesthetic block of the splanchnic nerves to determine before the operation whether it was through the left, through the right or through both splanchnic nerves that the afferent sensory fibers carrying the visceral painful sensations ran. By the use of this method, it was possible to obtain an accurate indication regarding the topography of the afferent painful pathways that pass through the splanchnic nerves and the probable result of unilateral or bilateral splanchnicectomy as treatment of visceral pain.

3. In Peptic Ulcer: Much evidence has been collected by several authors, particularly during the last years, that points out the probable role of the autonomic nervous system in the pathogenesis of peptic ulcer. It was demonstrated that in certain brain tumors and following hypothalamic lesions caused by operations on the brain (Cushing<sup>49</sup> and Grant<sup>50</sup>) gastroduodenal erosions, perforations or ulcers may occur. On the other hand, the role of emotions and of psychosomatic disturbances in the pathogenesis of peptic ulcer has been emphasized by several authors (Cushing,<sup>49</sup> Robinson,<sup>51</sup> Bolen,<sup>52</sup> Winkelstein and Rothschild,<sup>53</sup> Wolf<sup>54</sup> and Wolff<sup>55</sup>).

For several years Dragstedt<sup>56</sup> has been studying the problem of the pathogenesis of peptic ulcer. In a complete and interesting work published in 1942, he emphasized his belief that "the problem of the cause of gastric and duodenal ulcer is a part of the more general question of the resistance of the gastrointestinal tract to the digestive action of its own secretions." In the same year, Palmer<sup>57</sup> pointed out that the problem of peptic ulcer in man is one of tissue resistance versus acid attack. The point of view of these authors seems to be in exact accord with the

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49. Cushing, H.: Peptic Ulcers and Interbrain, Surg., Gynec. & Obst. **55**:1, 1932.

50. Grant, F. C.: Brain Lesions and Duodenal Ulcer: Report of Two Cases, Ann. Surg. **101**:156, 1935.

51. Robinson, S. C.: Role of Emotions in Gastroduodenal Ulcers, Illinois M. J. **71**:338, 1937.

52. Bolen, H. L.: The Emotional Factor in Peptic Ulcer, Rev. Gastroenterol. **10**:187, 1943.

53. Winkelstein, A., and Rothschild, L.: Some Clinical Studies on the Psychosomatic Background of Peptic Ulcer, Am. J. Digest. Dis. **10**:99, 1943.

54. Wolf, S., and Wolff, H. G.: Human Gastric Function, New York, Oxford University Press, 1943.

55. Wolff, H. G.: Emotions and Gastric Function, Science **98**:481, 1943.

56. Dragstedt, L. R.: Pathogenesis of Gastroduodenal Ulcer, Arch. Surg. **44**: 438 (March) 1942.

57. Palmer, W. L.: Peptic Ulcer and Gastric Secretion, Arch. Surg. **44**:452 (March) 1942.

present interpretation of the problem of peptic ulcer and includes the two factors which must be considered when the pathogenic mechanism of peptic ulcer is analyzed: (1) the gastroduodenal wall and its power of resistance versus (2) the peptic activity of the gastric secretion. Probably the mechanism of peptic ulcer is variable from case to case, and in every one the principal role is played by one or both of these factors.

The vagal neurogenic conception of gastric hypersecretion was accepted by Dragstedt and Owens,<sup>58</sup> who in 2 cases of duodenal ulcer performed supradiaphragmatic section of the vagus nerves. From the study of the 2 patients, the authors concluded that the data obtained indicate that the excessive night secretion of gastric juice in patients with ulcer is probably neurogenic in origin and may be greatly reduced by supradiaphragmatic section of the vagus nerves.

In 1945 Dragstedt and Schafer<sup>59</sup> reported the results that they had obtained in 13 patients with duodenal ulcer, in 1 patient with gastric ulcer and in 1 with gastrojejunal ulcer following supradiaphragmatic division of the vagus nerves. The patient with gastric ulcer has been apparently cured of his disease, and all but 1 of the patients with duodenal ulcer have been greatly improved or cured, although 3 patients have required gastroenterostomy because of persistence of obstructive symptoms. The patient with gastrojejunal ulcer, although improved, has been continued on medical management. In these patients the excessive continuous night secretion of gastric juice has been greatly reduced by the vagus section, a fact which, according to Dragstedt and Schafer, favors the conception that this abnormality is neurogenic in origin and the view that gastroduodenal ulcer is a psychosomatic disease. I was especially interested in the study of the first factor, the resistance of the gastroduodenal wall. I started from the hypothesis that if the decreased resistance of the gastroduodenal wall favors the genesis of peptic ulcer the progressive increase of resistance of the same wall must speed the healing of an existing ulcer. To increase locally the resistance of the gastroduodenal wall, I exerted action on the blood supply by temporary or definitive interruption of the vasomotor innervation of the stomach and duodenum. By repeated anesthetic blocks or by splanchnicectomy, I interrupted the splanchnic nerves in patients with ulcers, and a favorable result was observed.<sup>60</sup>

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58. Dragstedt, L. R., and Owens, F. M.: Supradiaphragmatic Section of the Vagus Nerves in the Treatment of Duodenal Ulcer, *Proc. Soc. Exper. Biol. & Med.* **53**:152, 1943.

59. Dragstedt, L. R., and Schafer, P. W.: Removal of the Vagus Innervation of the Stomach in Gastroduodenal Ulcer, *Surgery* **17**:742, 1945.

60. de Sousa Pereira, A.: O tratamento das úlceras gastro-duodenais pelos bloqueios anestésicos dos nervos esplâncnicos, *Portugal méd.*, 1942, no. 1, p. 1.

At the same time, I have approached this problem on an experimental basis.<sup>61</sup> In a series of 30 dogs under general ether anesthesia and after previous gastrotomy, my co-workers and I<sup>61</sup> have made wounds in the gastric mucosa. The diameters of those wounds varied—1.50 cm. in 3 dogs, 2 cm. in 18 dogs and 5 cm. in the last 9 dogs. The wounds embraced the full thickness of the gastric mucosa. In 20 of these animals the wound was made in the antrum, in 7 in the region of the fundus and in 3 at the pylorus. In 13 dogs only resection of the gastric mucosa in the regions just mentioned was done. In 16 dogs, after the gastric wound was made, unilateral splanchnicectomy was performed, and in 1 dog bilateral splanchnicectomy was done. All the animals were kept under observation for periods ranging from eight to thirty days and were then killed. It was observed that there was a remarkable



Fig. 11.—Wound of the gastric mucosa made in the region of the antrum. In the figure on the left (dog 1000), the wound is ten days old. In that on the right (dog 1002), the wound was followed by right splanchnicectomy and is nine days old.

acceleration of healing in the animals in which the wound of the gastric mucosa had been followed by splanchnicectomy (fig. 11).

The results of these experimental investigations are in accordance with the facts that I have observed in patients. In 3 cases of ulcer of the lesser curvature, I have performed repeated (eight to twenty) anesthetic blocks of the splanchnic nerves. These blocks were made during a period of nineteen to twenty-two days; and it was demonstrated by roentgenologic examination that the ulcer cavity had disappeared

61. de Sousa Pereira, A.; Rodrigues, A., and Carvalho, R.: A influência da interrupção dos nervos esplâncnicos sobre a cicatrização das feridas gástricas, Portugal méd., 1941, no. 1, p. 1.

during that period (fig. 12). Gastrectomy was then performed, and the gastric specimen was studied. The anatomic and histologic study in every case confirmed the advanced phase of healing and organization of the scar tissue in the spot where an ulcer cavity had been shown by roentgenogram before treatment (fig. 13).

Section of the splanchnic nerves causes interruption of the vasomotor fibers that pass through them. I tried to determine the influence of splanchnicectomy on the arterial collateral circulation of the stomach. In a series of 10 dogs the vessels at the level of the greater curvature were interrupted by ligation. In 5 dogs, interruption of these vessels was performed and the animals were kept under observation. In 5 other animals, interruption of the vessels of the greater curvature was followed by splanchnicectomy. These animals have been studied



Fig. 12.—Ulcer of the lesser curvature in a patient (F. R.) 31 years old. *A*, observation on Oct. 18, 1943, before treatment. *B*, observation on November 12, after twenty splanchnic nerve blocks made during twenty-two days. *C*, observation on December 3. Gastrectomy was done on November 15.

by arteriography one to four weeks after the operation. It was observed that in animals in which only the interruption of the vessels of the greater curvature was performed the development of the arterial collateral circulation was uniform through the entire area of the gastric wall (fig. 14), but in 5 dogs in which ligation of the vessels of the greater curvature was followed by splanchnicectomy there was a greater development in the arterial collateral circulation. In the two thirds of the stomach corresponding to the side of the interruption of the splanchnic nerves (fig. 15), the increase of collateral arterial supply was evident.

In April 1939 I began studying the influence of repeated anesthetic blocks of the splanchnic nerves in the treatment of peptic ulcer.<sup>60</sup> From that time until May 1944 I had studied carefully and closely a series of 18 patients with peptic ulcer: 8 with ulcer of the lesser curvature; 4

with pyloric or justapyloric ulcer; 2 with duodenal ulcer and 4 with multiple ulcers. In 17 of these patients it was possible by repeated anesthetic blocks of the splanchnic nerves, performed during periods varying from one to two months, to obtain relief of clinical signs and complete healing of the ulcer demonstrated in every case by the roentgenologic examination (figs. 16, 17 and 18). In 1 case in which there was a penetrating ulcer of the lesser curvature, no healing of the ulcer



Fig. 13.—Ulcer of the lesser curvature in a patient (F. R.) 31 years old. Gastrectomy specimen obtained after the treatment by twenty splanchnic nerve blocks made during twenty-two days. Histologic section of the scar of the gastric ulcer.

was obtained and only temporary relief of the epigastric pains. In these patients the periods of observation after the treatment ranged from six months to five years. In 1 case of ulcer of the lesser curvature in this series a recurrent lesion was observed a year later in a different point of the lesser curvature. A new series of anesthetic blocks of the splanchnic nerves quickly relieved the clinical signs and speeded the

healing of the ulcer. Also in 1 case of duodenal ulcer, a recurrent lesion was observed three years after the treatment. Repeated anesthetic blocks were performed, and the ulcer healed. Fifteen months later the patient still was in good condition. The pyloric and justapyloric ulcers

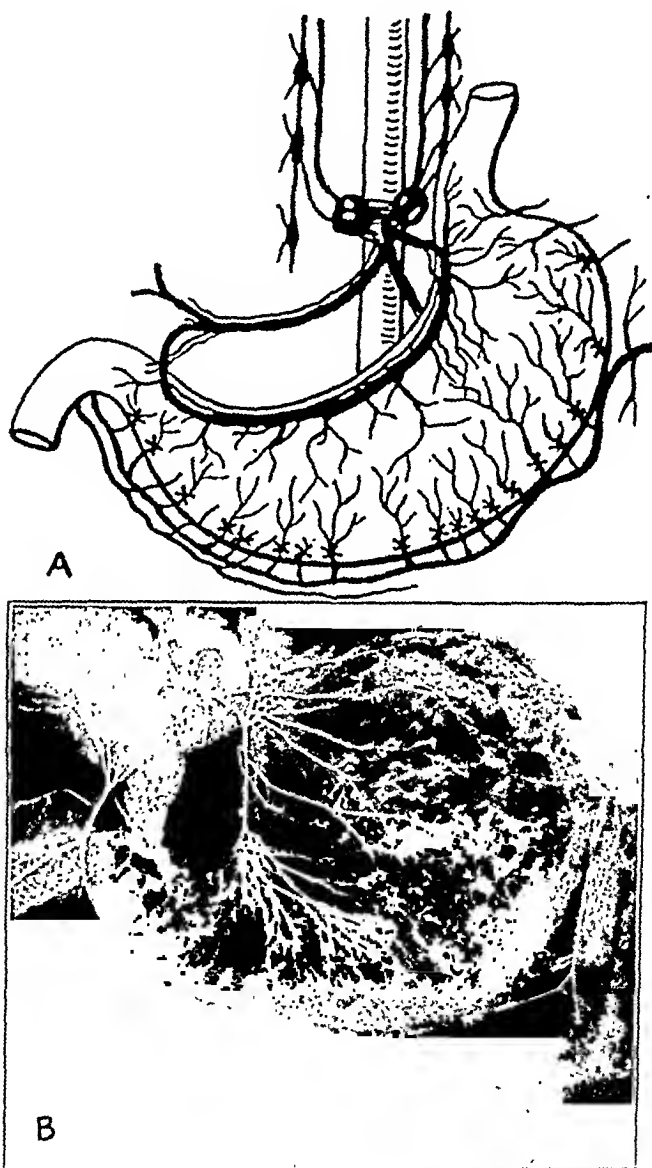


Fig. 14 (experiment 1, dog 988).—*A*, ligation of the vessels of the greater curvature of the stomach. *B*, arteriography done twenty-three days after operation. The collateral circulation developed between the arteries of the two curvatures is practically the same in the whole gastric area.

healed, but a pyloric stenosis appeared in 3 patients that needed surgical operation to relieve the stenosis.

The study of these cases showed that pain is quickly relieved and that peptic ulcer can be completely healed by increase of the arterial

blood supply of the gastroduodenal wall by repeated anesthetic blocks of the splanchnic nerves. Only in 1 patient of this series with a penetrating ulcer of the lesser curvature was this result not obtained. After I observed the recurrence of ulcer in 2 cases, I began, two years ago, to perform interruption of the splanchnic nerves by splanchnicectomy

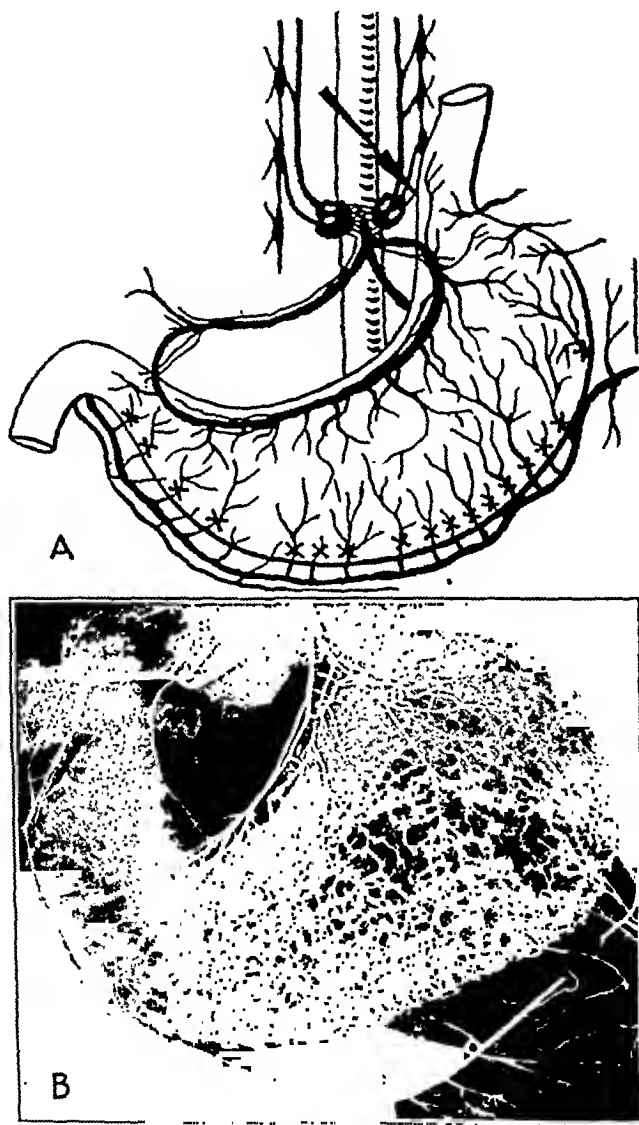


Fig. 15 (experiment 11, dog 981).—*A*, ligation of the vessels of the greater curvature followed by left splanchnicectomy. *B*, arteriography, twenty days after operation, shows a greater development of the collateral arterial circulation in the left two thirds of the stomach.

in cases of peptic ulcer. All experimental and clinical data of my investigations regarding the problem of peptic ulcer and autonomic nervous system will soon be published.



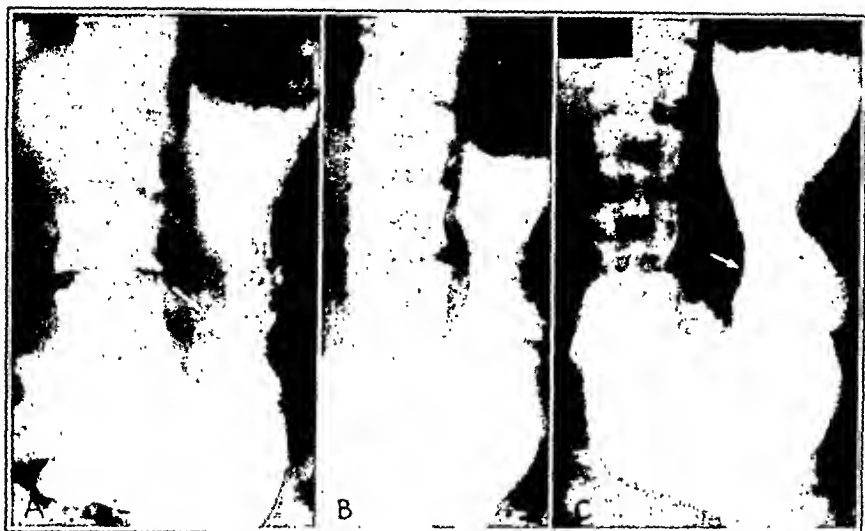


Fig. 16.—Ulcer of the lesser curvature in a patient (I. C.) 45 years old. *A*, observation on Oct. 23, 1943, before the treatment. *B*, observation on December 2, after twenty splanchnic nerve blocks practiced during twenty-four days. *C*, observation December 12, after twenty-six splanchnic nerve blocks practiced during thirty-four days.



Fig. 17.—Ulcer of the lesser curvature in a patient (M. P. B.) 49 years old. *A*, observation on Nov. 8, 1943, before treatment. *B*, observation on December 2, after sixteen splanchnic nerve blocks during twenty-two days. *C*, observation on December 17, after thirty splanchnic nerve blocks practiced during thirty-seven days.

II. *Anesthetic Block of the Splanchnic Nerves and First Lumbar Ganglion.*— 4. In Paralytic Ileus: The intestine is innervated by both parasympathetic and sympathetic nerves, the first activating and the latter exerting a tonic inhibitory influence (Pottenger<sup>33</sup>). Excitation of the splanchnic nerves causes inhibition of the intestine, affecting both longitudinal and circular coats (Bayliss and Starling<sup>62</sup>). Interruption of these nerves favors the intestinal motor activity of the opposing parasympathetic system. However, both the sympathetic nerves and the vagus nerves may conduct both motor and inhibitory impulses to



Fig. 18.—Multiple ulcers (ulcer of the lesser curvature and duodenal ulcer) in a patient (L. P.) 47 years old. *A*, observation on Oct. 9, 1942, before the treatment. *B*, observation on December 22, after thirty-one splanchnic nerve blocks during forty-nine days.

the gastrointestinal musculature. Bilateral section of the splanchnic nerves results in increased tone and augmented peristaltic activity of the gastrointestinal musculature (Kuntz<sup>32</sup>). This physiologic knowledge of the innervation of the intestine offers the basis for the treatment of paralytic ileus by anesthetic block of the intestinal sympathetic innervation.

62. Bayliss, W. B., and Starling, E. H.: The Movements and Innervation of the Small Intestine, *J. Physiol.* 24:99, 1899.

Several clinical reports have appeared since Wagner,<sup>63</sup> in 1922, made known the favorable results of spinal anesthesia in the treatment of ileus. Duval<sup>64</sup> reported that evacuation of the intestine was brought about in 68 per cent of the cases of adynamic, paralytic and spasmodic ileus. Markowitz and Campbell,<sup>65</sup> in experimental investigations, observed that the reflex paralysis of the bowel movements induced in dogs by laparotomy or by the intraperitoneal injection of iodine or by severe intra-abdominal traumatism is promptly abolished by spinal anesthesia induced by procaine hydrochloride. Ochsner, Gage and Cutting<sup>66</sup> suggested, in 1928, the treatment of ileus by the mere blocking of the splanchnic nerves. They performed twenty-five experiments on dogs to determine the effect of splanchnic anesthesia in ileus. They stated the belief that physiologic, chemical and paralytic ileus or mechanical ileus following the relief of an obstruction may be satisfactorily treated in the experimental animal by block of the splanchnic nerves. Rosenstein and Köhler<sup>67</sup> observed that in rabbits peristalsis was produced following the injection of large amounts of procaine hydrochloride solution into the splanchnic area. These experimental reports are favorable to the conception of treatment of paralytic ileus by anesthetic block of the intestinal sympathetic innervation.

Since 1938<sup>68</sup> I have routinely employed bilateral anesthetic block of the splanchnic nerves and first lumbar ganglion in every case in which a clinical diagnosis of paralytic ileus was made. It was observed that in some cases the physiologic interruption of the splanchnic nerves and first lumbar ganglion increased the peristaltic movements of the intestine and was followed after the treatment by intestinal discharge. In other cases, the effect was only partial and it was necessary to add other therapeutic methods to complete the effect of the anesthetic block. In a few cases it had no influence on the intestinal function. When the intestinal effect following the first anesthetic block was only partial or absent and it was necessary to prolong the action of the interruption

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63. Wagner, G. A.: Zur Behandlung des Ileus mit Lumbalanästhesie, Arch. f. Gynäk. **117**:336, 1922.

64. Duval, P.: La rachianesthésie dans l'occlusion intestinale, Bull. et mém. Soc. nat. de chir. **53**:477, 1927.

65. Markowitz, J., and Campbell, W. R.: The Relief of Experimental Ileus by Spinal Anesthesia, Am. J. Physiol. **81**:101, 1927.

66. Ochsner, A.; Gage, I. M., and Cutting, R. A.: Treatment of Ileus by Splanchnic Anesthesia: Preliminary Report of Experimental Study, J. A. M. A. **90**:1847 (June 9) 1928.

67. Rosenstein, P., and Köhler, H.: Therapeutische Versuche zur Bekämpfung der Darmlaemung durch Umspritzung des Ganglion coelicum, Med. Klin. **22**:530, 1926.

68. de Sousa Pereira, A.: A infiltração novocainica dos nervos esplancnicos na terapeutica da oclusão intestinal, Med. contemp., April 10, 1938.

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of the sympathetic innervation of the intestine, a second anesthetic block was performed after the effect of the first block had disappeared. If it was not followed by a favorable result when associated with other therapeutic methods a laparotomy was performed. In a few instances in which the anesthetic blocks of the splanchnic nerves had given unsuccessful results, a mechanical cause was found when the laparotomy was practiced. In the cases of paralytic ileus in which the anesthetic block was successful, daily repeated anesthetic blocks were performed at the level of the splanchnic nerves and first lumbar ganglion until complete reestablishment of the intestinal function was obtained. In all cases of ileus in which the patients were treated by anesthetic blocks, the general and local condition of the patient and especially the arterial blood pressure were carefully evaluated before and during the treatment because interruption of the splanchnic nerves is followed by hypotension.

5. In Megacolon: Both sympathetic and parasympathetic nerves innervate the colon. Schmidt,<sup>69</sup> experimenting on cats and dogs, observed that the vagus nerves supply the ascending and transverse portions of the colon whereas the sacral fibers are distributed to the entire colon. These results confirm the physiologic observations of Carlson<sup>70</sup> on the dog, in which irritation of the sacral nerves produces a motor effect on the circular and longitudinal musculature over the entire bowel. On the other hand, it is admitted at the present time (Pottenger<sup>83</sup>) that the sympathetic pathways for the colon come through the lower thoracic and upper lumbar segments of the cord and reach the colon through the superior and inferior mesenteric ganglions.

Since Wade and Royle<sup>71</sup> have observed improvement in bowel activity following lumbar ramisection in cases of spastic paraplegia, different types of sympathetic operations have been performed in the treatment of megacolon. Judd and Adson<sup>72</sup> obtained satisfactory results from lumbar sympathetic ganglionectomy and ramisectomy in the treatment of 2 patients suffering from congenital idiopathic dilatation of the colon. Rankin and Learmonth<sup>73</sup> performed resection of the inferior

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69. Schmidt, C. A.: Distribution of Vagus and Sacral Nerves to the Large Intestine, *Proc. Soc. Exper. Biol. & Med.* **30**:739, 1933.

70. Carlson, A. J.: The Extrinsic Nervous Control of the Large Bowel, *J. A. M. A.* **94**:78 (Jan. 11) 1930.

71. Wade, R. B., and Royle, N. D.: The Operative Treatment of Hirschsprung's Disease: New Method with Explanation of the Technic and Results, *M. J. Australia* **1**:137, 1927.

72. Judd, E. S., and Adson, A. W.: Lumbar Sympathectomy and Ramisectomy for Congenital Idiopathic Dilatation of the Colon, *Ann. Surg.* **88**:479, 1928.

73. Rankin, F. W., and Learmonth, J. R.: The Present Status of the Treatment of Hirschsprung's Disease, *Am. J. Surg.* **15**:219, 1932.

mesenteric and presacral nerves in 8 cases, with return of the function of the colon, although tardily in some cases. Barrington-Ward<sup>74</sup> carried out the same operation in 2 cases, with good results. Adson<sup>75</sup> and Leriche<sup>76</sup> in the same year introduced splanchnicectomy alone or accompanied with lumbar sympathectomy in the treatment of megacolon. Leriche and co-workers<sup>77</sup> obtained favorable results in patients in whom this type of sympathetic denervation of the colon was performed.

Spinal anesthesia as a test of sympathetic overactivity was introduced by Scott and Morton.<sup>78</sup> In 2 clinical cases of Hirschsprung's disease they have demonstrated the immediate augmentation in motor activity of the large bowel on the induction of spinal anesthesia. They have proposed the adoption of this procedure to ascertain in any individual case of megacolon how effective operative interruption of its sympathetic innervation will prove to be.

The difficulties that I have encountered in the indication for splanchnicectomy and lumbar sympathectomy in cases of Hirschsprung's disease led me to study, as a preoperative test, the physiologic interruption of the splanchnic nerves and first lumbar ganglion by repeated anesthetic blocks. Three cases of megacolon were studied by this method. Daily repeated anesthetic blocks of the splanchnic nerves and first lumbar ganglion were performed alternately in the right and left sides during a period of two weeks. These patients were studied clinically and by roentgenographic examination before, during and after the treatment in similar technical conditions in order that the results might be compared. This study showed in these cases that repeated anesthetic blocks were followed by functional and morphologic improvement of the colon. Splanchnicectomy and resection of the first lumbar sympathetic ganglion were then performed. These 3 patients with megacolon were operated on according to the indication of this test. The immediate results obtained and those which followed during a period of observation ranging from five months to two years have been encouraging. The small number of cases, however, and the short period of observation do not permit a definitive conclusion.

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74. Barrington-Ward, L. E.: Abdominal Sympathectomy for Hirschsprung's Disease, *Proc. Roy. Soc. Med.* **25**:1221, 1932.

75. Adson, A. W.: Hirschsprung's Disease: Indications for and Results Obtained by Sympathectomy, *Surgery* **1**:859, 1937.

76. Leriche, R.: De la section des splanchniques dans le mégacolon non compliqué avec ou sans dolichocolon, *Presse méd.* **45**:1851, 1937.

77. Leriche, R.; de Sousa Pereria, A., and DeBailey, M.: La resection des nerfs splanchniques: Technique et resultats de quelques observations de thrombo-angeite oblitérante, hypertension paroxystique, megacolon et dolichocolon, *Med. contemp.* no. 27, 1937.

78. Scott, J. M., and Morton, J. J.: Sympathetic Inhibition of the Large Intestine in Hirschsprung's Disease, *J. Clin. Investigation* **9**:247, 1930.

6. In Hypertension: Although the cause and mechanism of essential hypertension remain unknown, great progress has been made during recent years in the surgical treatment of this disease. According to White and Smithwick,<sup>40</sup> the most important factors in this disease seem to be primary vascular disease, sympathetic outflow from cerebral centers, normal endocrine activity and the presence of an angiospastic humoral substance.

Since Kraus suggested to Brünning<sup>79</sup> the surgical approach to the problem of hypertension, investigations have been made by Daniélopou,<sup>80</sup> Pieri,<sup>81</sup> Adson and Allen,<sup>82</sup> Craig,<sup>83</sup> Peet,<sup>84</sup> Leriche,<sup>76</sup> Crile,<sup>85</sup> Dandy<sup>86</sup> and Smithwick<sup>87</sup> to find a method of surgical treatment of this disease through extensive sympathectomy. Four types of sympathectomy are in common use today: subdiaphragmatic sympathectomy (Adson and Allen, Craig and Leriche), supradiaphragmatic splanchnicectomy and lower dorsal sympathetic ganglionectomy (Peet), celiac ganglionectomy (Crile) and thoracolumbar sympathectomy (Smithwick, Dandy and

79. Kraus and Brünning, cited by White and Smithwick.<sup>40</sup>

80. Daniélopou, D.: *Chirurgie du système végétatif*, Bull. méd. **37**:988, 1923.

81. Pieri, G.: La resezione dei nervi splanchnici: Contributo tecnico alla chirurgia del sistema nervoso vegetativo, Ann. ital. di chir. **6**:678, 1927; Tentativi di cura chirurgica dell'ipertensione arteriosa essenziale, Riforma med. **48**:1173, 1932.

82. Adson, A. W., and Allen, E. V.: Essential Hypertension: General Considerations and Report of Results of Treatment by Extensive Resection of Sympathetic Nerves and Partial Resection of Both Suprarenal Glands, in Collected Papers of the Mayo Clinic, Philadelphia, W. B. Saunders Company, 1936, vol. 28, p. 1001. Allen, E. V., and Adson, A. W.: Physiologic Effects of Extensive Sympathectomy for Essential Hypertension: Further Observations, Ann. Int. Med. **11**:2151, 1938.

83. Craig, W. M.: Surgical Approach to and Resection of the Splanchnic Nerves for Relief of Hypertension and Abdominal Pain, West. J. Surg. **42**:146, 1934; Hypertension: A Consideration of Its Surgical Treatment, Brit. M. J. **2**:1215, 1939. Craig, W. M., and Adson, A. W.: Hypertension and Subdiaphragmatic Sympathetic Denervation, S. Clin. North America **19**:969, 1939.

84. Peet, M. M.: The Surgical Treatment of Hypertension, J. internat. de chir. **5**:1, 1940. Peet, M. M.; Woods, W. W., and Braden, S.: The Surgical Treatment of Hypertension: Results in 350 Consecutive Cases Treated by Bilateral Supradiaphragmatic Splanchnicectomy and Lower Dorsal Sympathetic Ganglionectomy, J. A. M. A. **115**:1875 (Nov. 30) 1940.

85. Crile, G.: The Surgical Treatment of Hypertension, edited by A. Rowland, Philadelphia, W. B. Saunders Company, 1938, p. 237; Operative Treatment of Essential Hypertension, South. Surgeon **7**:220, 1938; Progress Notes on the Treatment of Essential Hypertension by Celiac Ganglionectomy, S. Clin. North America **19**:1205, 1939.

86. Bordley, J., III; Galdston, M., and Dandy, W. E.: The Treatment of Essential Hypertension by Sympathectomy, Bull. Johns Hopkins Hosp. **72**:127, 1943.

87. Smithwick, R. R.: A Technique for Splanchnic Resection for Hypertension, Surgery **7**:1, 1940.

Poppen<sup>88</sup>). All these operations have the purpose of interrupting more or less extensively the sympathetic pathways between the thoracolumbar sympathetic chain and the celiac and mesenteric plexuses. Analysis of the results thus far obtained in the surgical treatment of hypertension shows that in certain patients the blood pressure can be lowered in a significant manner by splanchnicectomy. White and Smithwick<sup>40</sup> pointed out that at the present time great emphasis should be placed on the selection of cases for sympathectomy. All factors that may be of value in prediction of a favorable effect from operation must be considered. They emphasized the point that the best index is the reduction in blood pressure.

As the sympathetic operation in the treatment of hypertension causes lowering in blood pressure by interruption of the sympathetic pathways, it is logical to determine preoperatively the effect that follows the temporary interruption of the same sympathetic nerves. On this basis I have tried and I use in cases of hypertension the anesthetic block of the splanchnic nerves and first lumbar ganglion as a preoperative test before performing splanchnicectomy. The anesthetic block is first performed on the left side, the next day on the right side and on the third day bilaterally. The curves of the arterial blood pressure are studied during and between the anesthetic blocks. It was observed that anesthetic block is followed by an immediate effect on the blood pressure, lasting about one hour. The effect obtained is equivalent to that which follows immediately the surgical interruption of the splanchnic nerves and first lumbar ganglion at the same level. This test gives useful indication in each case of hypertension as to the probable result of splanchnicectomy.

It must be remembered that anesthetic block gives information regarding only the immediate vasomotor effect that follows interruption of the splanchnic nerves and the first lumbar ganglion. In experiments carried out on dogs<sup>89</sup> to determine the influence of anesthetic block and of sympathectomy of the lumbar sympathetic chain on the development of the collateral circulation of the lower extremities, we have observed that in the first hours after interruption of the sympathetic pathways the effect on the development of the collateral arterial circulation is similar. However, the study of other dogs weeks or months after lumbar sympathectomy showed that the development of the arterial collateral circulation in the posterior extremities was greater than that in the animals observed only a few hours after interruption of the

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88. Poppen, J.: Personal communication to the author.

89. de Sousa Pereira, A.; Rodrigues, A., and Carvalho, R.: La sympathectomie lombaire, l'infiltration novocaïnique lombaire, l'injection intra-artérielle de novocaïne, la résection unilatérale des nerfs splanchniques et la valeur comparée de l'effet de ces interventions sur le développement de la circulation collatérale des membres, *Presse méd.* 47:1545, 1939.

sympathetic chain. These experiments suggest that anesthetic block gives an immediate result comparable with the one observed immediately after the same sympathetic nerves are surgically interrupted. Later, however, sympathectomy is followed by a greater development of the arterial collateral circulation. This problem is under study, and the results observed will be presented.

7. In the Postoperative Period of Abdominal Operations: After abdominal operations there is some paresis of the intestine, so that gas does not pass along the bowel to be expelled properly, which may cause distention, pain and at times vomiting (Davis and Hansen <sup>90</sup>). On the other hand, the visceral operative wound during the postoperative period may cause pain produced by the stimulation of the sensory innervation. One of the consequences of visceral pain in the postoperative period is the diminution of the motility of the diaphragm, reducing pulmonary ventilation and favoring pulmonary complications. Complications occur in a much higher percentage after operations on the upper part of the abdomen.<sup>91</sup> In 90 per cent of cases, postoperative pulmonary complications are dependent on the general preoperative condition of the patient and are caused by the excessive formation of bronchial secretion and the retention of this secretion in the bronchi as a result of the operation (King <sup>92</sup>). It was emphasized by Keith <sup>93</sup> that the diaphragm plays an important part in facilitating ventilation of the lower pulmonary lobes, and it was shown by Head,<sup>94</sup> Powers,<sup>95</sup> Carlson <sup>96</sup> and Beecher <sup>97</sup> that pulmonary hypoventilation, with reduction of vital capacity and decreased diaphragmatic excursions, occurs commonly after abdominal operations. Restriction of respiration is an important factor in the cause of postoperative pneumonia (Sise, Mason and Bogan <sup>98</sup>), and the

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90. Davis, H. H., and Hansen, T. M.: Investigation of the Cause and Prevention of Gas Pains Following Abdominal Operations, *Surgery* **17**:492, 1945.

91. Churchill, E. D.: Pulmonary Atelectasis with Special Reference to Massive Collapse of the Lung, *Arch. Surg.* **11**:489 (Oct.) 1925.

92. King, D. S., in Mason, R. L.: Preoperative and Postoperative Treatment, Philadelphia, W. B. Saunders Company, 1937, p. 192.

93. Keith, A.: The Mechanism of Respiration in Man, in Hill, L.: Further Advances in Physiology, New York, Longmans, Green & Co., 1909, p. 182.

94. Head, J. R.: The Effect of Operation Upon the Vital Capacity, *Boston M. & S. J.* **197**:83, 1927.

95. Powers, J. H.: Vital Capacity: Its Significance in Relation to Postoperative Pulmonary Complications, *Arch. Surg.* **17**:304 (Aug.) 1928.

96. Carlson, H. A.: Changes in Respirations Produced by Surgical Operations, *Proc. Soc. Exper. Biol. & Med.* **29**:23, 1931.

97. Beecher, H. K.: The Measured Effect of Laparotomy on the Respiration, *J. Clin. Investigation* **12**:651, 1933.

98. Sise, L. F.; Mason, R. L., and Bogan, I. K.: Prophylaxis of Postoperative Pneumonia: Preliminary Report of Some Experiments After Upper Abdominal Operations, *Anesth. & Analg.* **7**:187, 1928.



varying degrees of partial atelectasis which occur after operations on the upper part of the abdomen are due primarily to diaphragmatic elevation and restriction (Muller, Overholt and Pendergrass<sup>99</sup>). The restriction of pulmonary ventilation appears to be caused by the operative wound which directly and reflexly interferes with abdominal and diaphragmatic excursions (Gius<sup>100</sup>).

Postoperative atelectasis is more frequent and is better explained on a mechanical than on an infectious basis (Blalock<sup>101</sup>), and it is believed that it results from the combined action of weakened respiratory force and bronchial obstruction (Churchill<sup>102</sup>). According to Elliot and Dingley,<sup>103</sup> obstruction of the bronchioles and the reflex immobility of the diaphragm play an important part in the causation of atelectasis. In the postoperative bronchopulmonary infectious complications, the bronchogenous mechanism acts either through the irritating effect of anesthetics administered by inhalation or by stagnation of its contents in the airways. This stagnation results from the inhibitory action of the pain, the forced immobilization and the diminished pulmonary ventilation. The retention of secretions in the tracheobronchial tree is caused by several factors. Inability to cough effectively appears as chief among these (Blalock<sup>101</sup>). Pain at the level of the operative wound in operations on the upper part of the abdomen is a cause of the inability of the patients to cough. All the facts mentioned point out the important influence of pain in the mechanism of atelectasis and other postoperative pulmonary complications.

Attempts have already been made by some authors to find the most adequate method for reduction or elimination of postoperative pain by physiologic interruption of the pathways of painful sensations between the area of the operative wound and the spinal cord. Crile<sup>104</sup> advised the injection of anesthetic solution (quinine and urea hydrochloride) around the operative wound, which produces analgesia for several days to a week. This method, however, was discarded because it produced fibrinous exudates, with an occasional tendency to suppuration at the

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99. Muller, G. P.; Overholt, R. H., and Pendergrass, E. P.: Postoperative Pulmonary Hypoventilation, *Arch. Surg.* **19**:1322 (Dec.) 1929.

100. Gius, J. A.: Paravertebral Procaine Block in the Treatment of Postoperative Atelectasis, *Surgery* **8**:832, 1940.

101. Blalock, A.: *Principles of Surgical Care: Shock and Other Problems*, St. Louis, C. V. Mosby Company, 1940.

102. Churchill, E. D., and McNeil, D.: The Reduction in Vital Capacity Following Operation, *Surg., Gynec. & Obst.* **44**:483, 1927.

103. Elliot, T. R., and Dingley, L. A.: Massive Collapse of the Lungs Following Abdominal Operations, *Lancet* **1**:1305, 1914.

104. Crile, W. A., cited by Allen, C. W.: *Local and Regional Anesthesia*, ed. 2, Philadelphia, W. B. Saunders Company, 1918, p. 205.

sites of injection. Later Capelle<sup>105</sup> recommended in surgical wounds the continuous administration of procaine hydrochloride to relieve pain and to increase the postoperative vital capacity. In 2 cases of atelectasis following appendectomy in children, Gius<sup>100</sup> obtained remarkable therapeutic results with paravertebral anesthetic block of the operative wound. This procedure allows active hyperventilation of the lungs and effective coughing. The 2 patients were successfully treated by this method. In a series of 8 patients who had had operations on the biliary tract, Starr and Gilman<sup>106</sup> performed anesthetic blocks of the sixth to tenth intercostal nerves according to the technic described by Bartlett.<sup>107</sup> Following the intercostal nerve block, anesthesia persisted for three or four hours and analgesia for more than twenty-four hours. When abdominal pain returned, it was mild in every case. In these patients postoperative pain in wounds in the upper part of the abdomen was relieved, coughing was easier and more effective and there was an increase in pulmonary ventilation. In 15 patients Zollinger<sup>108</sup> practiced anesthetic block, according to the technic of Bartlett,<sup>107</sup> of the sixth to eleventh intercostal nerves, with eucupine solution in oil to obtain anesthesia of the operative wound of the abdominal wall. In 20 cases of operations on the upper part of the abdomen, Belinkoff<sup>109</sup> tried postoperative block of the last intercostal nerves, with Novest-Oil (Monocaine [2-isobutylaminoethyl-*p*-aminobenzoate], benzyl alcohol, ethyl aminobenzoate and expressed oil of almond) as the anesthetic solution. He concluded that this method relieves the postoperative pain and favors pulmonary ventilation, reducing consequently the incidence of postoperative complications.

The role of pain in wounds of the abdominal wall in the mechanism of pulmonary hypoventilation and in the reduction of the diaphragmatic excursion has been already demonstrated (Churchill and McNeil<sup>102</sup>). However, in operations on the upper part of the abdomen, in addition to the parietal pain there is also a deep visceral pain at the level of the visceral wound. It has already been seen that the splanchnic nerves carry the afferent sensory pathways through which pass the painful sensations of the organs innervated by the solar plexus. During

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105. Capelle, W.: Die Bedeutung des Wundschmerzes und seiner Ausschaltung für den Ablauf der Atmung bei Laparotomierten, *Deutsche Ztschr. f. Chir.* **246**: 466, 1936.

106. Starr, A., and Gilman, S.: The Effect of Postoperative Intercostal Nerve Block on Pulmonary Ventilation, *New England J. Med.* **227**:102, 1942.

107. Bartlett, R. W.: Bilateral Intercostal Nerve Block for Upper Abdominal Surgery, *Surg., Gynec. & Obst.* **71**:194, 1940.

108. Zollinger, R.: Observations on the Use of Prolonged Anesthetic Agents in Upper Abdominal Incisions, *Surgery* **10**:27, 1941.

109. Belinkoff, S.: Intercostal Block with Long-Acting Anesthetic in Upper Abdominal Operations, *Anesthesiology* **5**:500, 1944.

splanchnicectomy performed with the patient under spinal anesthesia, Leriche<sup>45</sup> observed that mechanical stimulation of the upper end of the splanchnic nerves originated thoracic pain. I have verified the same fact in several patients in whom splanchnicectomy was performed while they were under local anesthesia. Repeated mechanical stimulations of the splanchnic nerves were followed by pain referred to the level of the thorax. This pain was completely absent when the same stimulations were repeated after anesthetic block of the splanchnic nerves. On the other hand, I have also demonstrated that in certain cases of angina pectoris precordial pain may be originated in stimulations arising at the level of the abdominal organs innervated by the solar plexus. The precordial pain was temporarily relieved by anesthetic block of the splanchnic nerves and definitively by splanchnicectomy.

The facts mentioned previously led me to try repeated anesthetic blocks of the splanchnic nerves to relieve during the postoperative period the visceral pain carried through the afferent sensory pathways of the splanchnic nerves. Two years ago I began studying the role of the sympathetic innervation in the postoperative period of abdominal operations in its relation to visceral pain and postoperative reflexes originating in the visceral wound. These investigations were carried on especially in operations on the upper part of the abdomen, performed in organs innervated by sympathetic branches of the solar plexus. Repeated anesthetic blocks of the splanchnic nerves and first lumbar ganglion were performed during the four or five days that followed the abdominal operation. Normally the first anesthetic block was performed twelve to twenty-four hours following the operation. The next blocks were performed every day on the left side, on the right side or bilaterally, according to the topography of the sympathetic innervation in relation to the topography of the visceral operative wound. These anesthetic blocks were repeated until the patient could breathe easily, without deep abdominal pain.

In 35 patients submitted to different abdominal operations (gastrectomy, gastroenterostomy, cholecystectomy, colectomy and appendectomy), this postoperative treatment of pain was routinely carried out. It was observed in these cases that the deep visceral pain was immediately and completely, although temporarily, relieved in every case after unilateral or bilateral anesthetic block of the splanchnic nerves, according to the topography of the visceral operative wound. During the relief of pain the patient could breathe deeply and cough more easily. After the first anesthetic block, pain reappeared but was not so intense as before the treatment. After repeated anesthetic blocks, the deep visceral pain was quickly relieved. The motility of the diaphragm following the anesthetic block of the splanchnic nerves showed an increase when the interruption of the splanchnic nerves and the first lumbar ganglion was

performed (fig. 19). In this series of abdominal operations (stomach, biliary tract, intestines and appendix), postoperative pulmonary complications or thrombophlebitis were not observed. The patients were turned frequently and encouraged to breathe deeply, and early ambulation, on the third or fourth day, was permitted for the greater number of these patients.

Another problem is being studied in connection with the relief of postoperative visceral pain and visceral reflexes. The problem is to know whether repeated anesthetic blocks of the sympathetic innervation performed during the postoperative period of the abdominal operations can be useful to prevent or to lessen the occurrence of postoperative phlebitis. It is admitted at the present time that interruption of the sympathetic innervation of the veins by repeated anesthetic blocks is a useful method in the treatment of postoperative phlebitis. Interruption of the sympathetic innervation of the veins in phlebitis and throm-

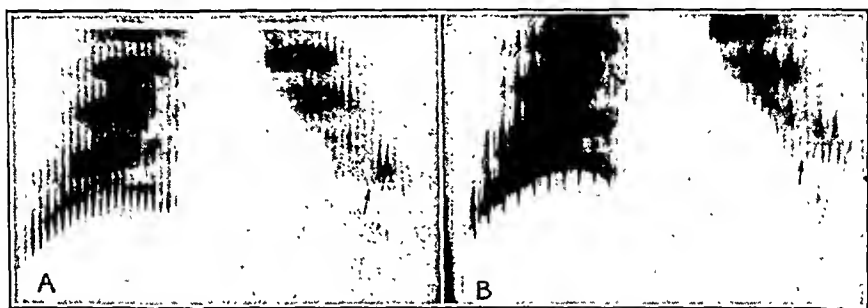


Fig. 19.—Ulcer of the lesser curvature in a patient on whom gastrectomy was performed. *A*, kymography of the diaphragm forty-four hours after gastrectomy. *B*, kymography on the same patient twenty minutes after the anesthetic block of the left splanchnic nerves. Note the increased amplitude of the left hemidiaphragm after the splanchnic block.

bophlebitis of the lower extremities is followed by relief from pain, relief from venospasm and increase in the collateral venous circulation.<sup>110</sup>

In 15 patients submitted to hysterectomy, the nature of the operation and the condition of the patients led to the supposition that phlebitis might occur as a postoperative complication. Anesthetic blocks of the splanchnic nerves and first lumbar sympathetic ganglion were repeated during one to two weeks, according to the postoperative progress of each patient. This treatment was associated with an early ambulation of these patients. In none of the cases did phlebitis occur. The results obtained in these few cases do not yet permit a conclusion; the problem continues under investigation.

110. de Sousa Pereira, A.: Innervation of the Veins: Its Role in Pain, Venospasm, and Collateral Venous Circulation, to be published.

## SUMMARY

Anesthetic block of the splanchnic nerves or of these nerves and the first lumbar ganglion has aroused in recent years a great interest in the study and solution of clinical problems related to these nerves.

Of the two routes of approach available today for the blocking of the splanchnic nerves, the posterior approach was practiced routinely in these investigations. When repeated anesthetic blocks were indicated, the needle was inserted not always at the same point, as advised in previous technics of other authors, but at different points in an area determined according to the topography of the splanchnic nerves and the first lumbar ganglion in relation to the skeleton.

The technic followed in the block of the splanchnic nerves and first lumbar ganglion is described, and the accidents observed with this anesthetic block are reported.

Although the clinical indications of single or repeated anesthetic blocks of the splanchnic nerves are still under investigation, encouraging results were obtained in the diagnosis and treatment of patients with cardiospasm, visceral pain and peptic ulcer.

Single or repeated anesthetic blocks of the splanchnic nerves and first lumbar ganglion were tried in cases of ileus paralyticus, megacolon, hypertension and in the postoperative period of abdominal operations as as method of diagnosis, as a method of treatment or as a test before splanchnicectomy.

The results already observed in these investigations point out the clinical importance of anesthetic block of the splanchnic nerves and first lumbar ganglion.

# PULMONARY SUCK AND BLOW AS A RESPIRATORY ANALEPTIC

Interdependence of Cardiac Massage and Suck and Blow Resuscitation

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IN considering the problem of resuscitation, one is prone to regard cardiorespiratory stimulants as chemical. The fact that certain analeptics may be purely mechanical or reflex in their *modus operandi* has received little or no clinical consideration. It is the purpose of this paper to present the results of studies supplementing a series of studies previously made by Thompson and Birnbaum<sup>1</sup> on a mechanical method of respiratory stimulation.

Mechanical devices have been used in pulmonary resuscitation since the middle of the sixteenth century, the time of Paracelsus,<sup>2</sup> who

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Read May 16, 1945, before the Surgical Division, Clinical Research Meeting, New York Academy of Medicine. The presentation was made by Dr. Joseph H. Fobes, director of the Graduate School of Surgery, New York Medical College, Flower and Fifth Avenue Hospitals.

Experimental studies were performed with the collaboration of Dr. Joseph A. Abbey, who is now a captain in the Medical Corps, Army of the United States.

Dr. S. A. Thompson gave invaluable suggestions during the course of these investigations.

1. (a) Birnbaum, G. L., and Thompson, S. A.: The Mechanism of Asphyxial Resuscitation, *Surg., Gynec. & Obst.* **75**:79 (July) 1942, (b) Thompson, S. A., and Birnbaum, G. L.: Phenomenon of Asphyxial Resuscitation: Resuscitation with Inert (Asphyxiating) Gases, *Proc. Soc. Exper. Biol. & Med.* **48**:203 Oct. 1941; (c) Resuscitation in Advanced Asphyxia, *J. A. M. A.* **118**:1364 (April 18) 1942; (d) The Phenomenon of Asphyxial Resuscitation, *Surg., Gynec. & Obst.* **74**:1078 (June) 1942; (e) Resuscitation in Advanced Asphyxia, *Surgery* **12**:284 (Aug.) 1942; (f) Asphyxial Resuscitation: The Phenomenon and Its Mechanism, *J. Thoracic Surg.* **12**:624 (Oct.) 1943; Comparative Value of Various Methods of Resuscitation, *Ann. Surg.* **120**:94 (July) 1944.

2. (a) E. and J. Resuscitator and Inhalator Acceptable, report of the Council on Physical Therapy, *J. A. M. A.* **112**:1945 (May 13) 1939. (b) Harrison, W.: A Brief Historical Review of the Employment of a Bellows as a Means of Inducing Artificial Respiration During the Three Hundred Years Which Elapsed Between A. D. 1530 and 1830, *Detroit M. J.* **16**:341 (Aug.) 1916.

utilized a fireside bellows. Present appliances fall into two main groups: (1) those of the Drinker type, applied externally to the thoracic wall, and (2) those of the pulmotor variety, which are utilized directly on the tracheobronchial tree. The latter, in turn, may be subdivided into appliances which inflate the lungs and those which utilize suction and/or inflation.

It is beyond the scope of this paper to enter into a detailed discussion of the pros and cons of the various mechanical methods. Most of the controversy centers on the desirability of active pulmonary deflation as opposed to that of dependence on passive elastic recoil of the lungs and thoracic wall for the accomplishment of exhalation. Thompson and Birnbaum, in their work as protagonists of suction in pulmonary resuscitation, have recently shown that alternating suction-inflation causes a reflex stimulus to respiration. To demonstrate this fact they utilized an inert asphyxiant gas—nitrogen or helium—in order to avoid any possible respiratory stimulation by the gas itself. This has been described by them as the “phenomenon of asphyxial resuscitation.” Expressed differently, one might say that they demonstrated the existence of a mechanical or reflex respiratory analeptic.

That the application of suction alone to the trachea and bronchi is a potent respiratory stimulant is shown in figure 2. It will be seen that each of a series of suction strokes causes an inspiratory gasp, irrespective of the phase of respiration. No such effect takes place with a similar series of pressure strokes. In other words, suction is utilized as a stimulus, not, as Henderson expressed the opinion, as a means of aspirating gas from the lungs.<sup>3</sup>

External methods of artificial respiration (manual and mechanical) do not stimulate; they merely duplicate respiratory movements until the normal physiologic nervous and chemical elements in control are able to take effect. Mechanical devices applied externally serve only as substitutes for prolonged manual artificial respiration and, as such, are not stimulatory. It should be repeated and reemphasized that the mechanical devices which act directly on the pulmonary tree, particularly in the application of suction, are stimulatory and not substitutive.

Concerning cardiac resuscitation, it can probably be said with assurance that this may most effectively be accomplished by direct manual stimulation of the heart. Both Coryllos<sup>4</sup> and Birnbaum and Thompson<sup>1a</sup> have demonstrated the importance of maintaining pulmonary ventilation during massage. However, several of my experiments (fig. 1) indicate that such a combination would frequently be inadequate if either pressure

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3. Henderson, Y., and Turner, J. M.: Artificial Respiration and Inhalation, *J. A. M. A.* **116**:1508 (April 5) 1941.

4. Coryllos, P. N.: Mechanical Resuscitation in Advanced Forms of Asphyxia, *Surg., Gynec. & Obst.* **66**:698 (April) 1938.

alone or suction alone were applied to the respiratory passages. Both suction and inflation should be utilized with cardiac massage.

#### PHYSIOLOGY OF RESPIRATION

Control of respiration is both reflex and chemical, and both mechanisms exert their influence on the respiratory center. Nervous control is mediated chiefly through the vagi, the influence of which is inhibitory; section of these nerves abolishes their inhibitory control. Both inflation and deflation reflexes have been demonstrated. However, under ordinary conditions only the inflation reflex is functional. During suction deflation a new set of end organs comes into play; these are more effective in resuscitation than are the stretch receptors of inflation.<sup>1a, f</sup> Galvanometric studies on the distal cut end of the vagus demonstrate the presence of action currents on inflation and suction but none on mere passive expiration.<sup>5</sup> Resuscitation by suck and blow fails to occur after the vagi are sectioned.

Chemical control is exerted chiefly by the relative concentrations of carbon dioxide and oxygen. Pulmonary ventilation is increased by carbon dioxide stimulation of the respiratory center. However, the center is said to be depressed by carbon dioxide in the presence of asphyxia.<sup>1a</sup>

#### ASPHYXIA

A complete discussion on the mechanism of asphyxia will not be entered on. Lougheed, Janes and Hall<sup>6</sup> found that in asphyxiated dogs the critical interval after the cessation of respiration was eleven to seventeen seconds.

Thompson and Birnbaum<sup>1f</sup> stated that the critical point for spontaneous recovery falls within thirty to forty-five seconds; in most cases an extension of only a few seconds rendered recovery impossible, even with manual artificial respiration combined with oxygen-carbon dioxide mixtures. On the other hand, a delay of one half to two and three-fourths minutes is possible, with recovery, if suck and blow is substituted for manual methods.

Four phases of asphyxia are mentioned by Coryllos.<sup>4</sup> These phases are, successively: (1) initial apnea, in which blood pressure rises and the breath is held, with or without spasm of the glottis; (2) dyspnea, characterized by labored, increased respiratory movements, with utilization of the accessory muscles of respiration, continued rise of blood pressure and perhaps tonic and clonic convulsions; (3) terminal apnea, with respiratory cessation, drop in blood pressure, loss

5. Birnbaum and Thompson.<sup>1a</sup> Thompson and Birnbaum.<sup>1e, f</sup>

6. Lougheed, D. W.; Janes, J. M., and Hall, G. E.: *Physiological Studies in Experimental Asphyxia and Drowning*, *Canad. M. A. J.* **40**:423 (May) 1939.



of muscle tone, pupillary dilatation and areflexia, with loss of sphincter control, and (4) cardiac failure, characterized by either ventricular standstill or fibrillation.

Manual artificial respiration at the end of phase 3 is ineffective, but suck and blow at this time causes a rise in blood pressure within thirty seconds. If pulmonary ventilation is maintained after cardiac arrest, then cardiac massage is effective even ten minutes later.

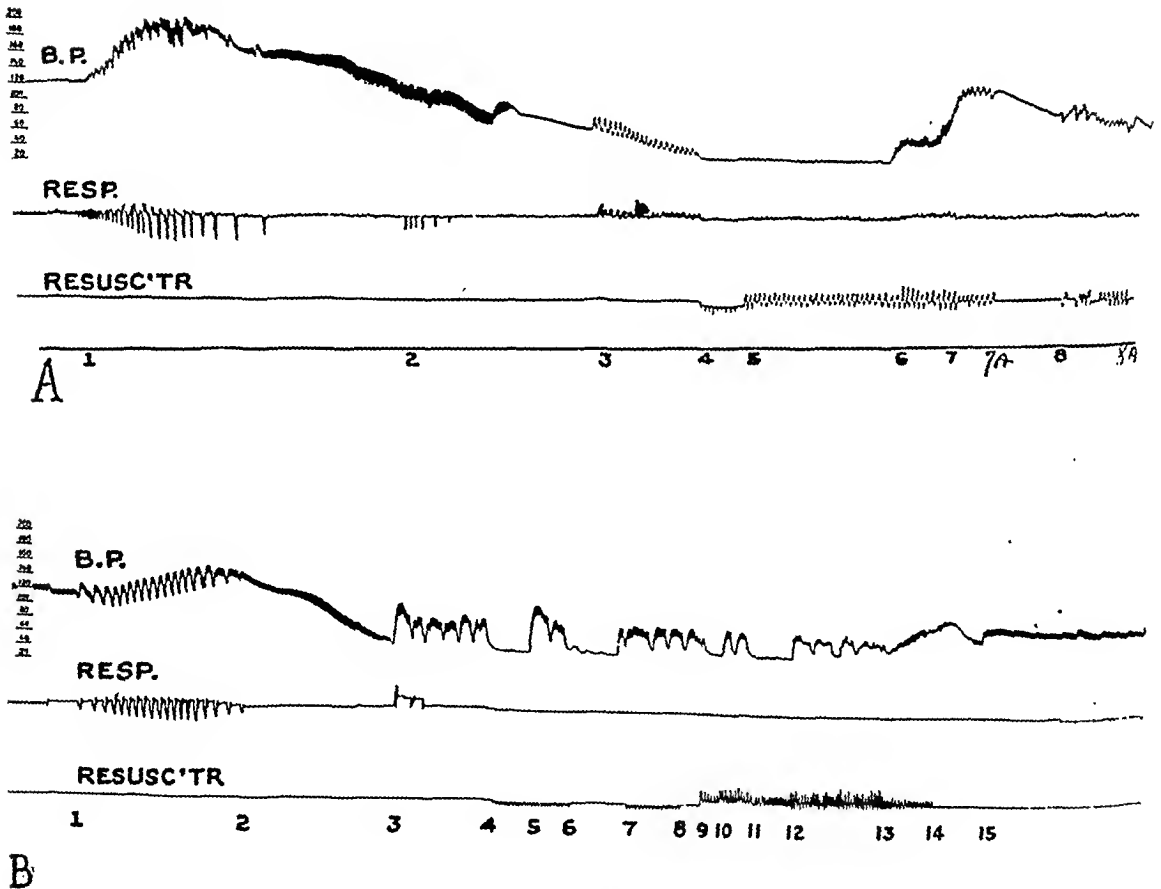


Figure 1

(See legend on opposite page)

#### HISTORY OF SUCK AND BLOW DEVICES

John Hunter<sup>7</sup> first used a double-chambered bellows experimentally as a suction-inflation resuscitator in 1755, and he recommended its use clinically in 1776. The use of a single-chambered fireside bellows for insufflation was popular in Europe and had been mentioned by Paracel-

7. Hunter, J.: Works, edited by J. F. Palmer, London, Longman [and others], 1837, vol. 3.

sus in 1560.<sup>2</sup> Courtois<sup>8</sup> in 1790 devised a hand-operated suck and blow pump, which he called *pompe apodopnique*, literally, a resuscitation pump. This is the earliest forerunner of the lungventilator, used in my experiments.

#### EXPLANATION OF PLATE.

Fig. 1.—*A*, The experiment demonstrates successful cardiac resuscitation by means of transdiaphragmatic massage together with inflation and deflation of the lungs. Air was used in the series of experiments presented in this paper. Resuscitation was accomplished after several other methods had failed. The top line represents the blood pressure, the middle line the respiration and the third the lung ventilator. At 1 obstructive asphyxia was produced by clamping the endotracheal tube. At 2 a few terminal gasps occurred and then respirations ceased. At 3 manual artificial respiration was attempted, without success, and the blood pressure continued to fall. At 4 suction and release were instituted by use of the suction tube of the apparatus and were continued to 5, without success. During these periods there did not appear to be any heart beat. At 5 positive inflation and negative deflation of the lung were instituted up to 6, without success.

At 6 a high midline incision was made in the abdomen and two fingers were slipped under the diaphragm; transdiaphragmatic massage was instituted at the same time that inflation and deflation of the lungs were continued. Notice the almost immediate resuscitation of the cardiovascular system; the elevation of the blood pressure was maintained. At 7 cardiac massage was discontinued. At 7A the use of the lungventilator was discontinued. Notice the downward trend of the blood pressure. At 8 a few more strokes of the lungventilator were instituted, and then they were discontinued at 8A, as recovery appeared to be maintained.

This experiment shows the necessity of cardiovascular resuscitation as well as respiratory resuscitation in the late stages of asphyxia. Three immediately preceding methods of respiratory resuscitation had failed completely to resuscitate the animal, although they did produce pulmonary ventilation. Without this pulmonary ventilation, cardiac massage would not have been successful. *B*, this experiment again demonstrates the necessity of cardiovascular as well as respiratory resuscitation in the late stages of asphyxia. Figure 1 demonstrates the failure of respiratory resuscitation alone and cardiac resuscitation alone and their success when combined. It also shows the necessity for pulmonary suck and blow ventilation in successful cardiac resuscitation. The technic is similar to that described in *A*. The top line represents the blood pressure, the middle line represents the respiration and the bottom line represents the lungventilator. At 1 tracheal obstruction is produced by clamping the endotracheal tube. At 2 respirations have ceased. At 3, through a median abdominal incision, transdiaphragmatic cardiac massage is attempted, no pulmonary ventilation being used, and is unsuccessful. At 4 suction and release alone is used and is unsuccessful. At 5 suction is combined with transdiaphragmatic cardiac massage and is unsuccessful. Suction is discontinued at 6; suction and transdiaphragmatic cardiac massage are again continued, from 7 to 8, but are unsuccessful. At 9 inflation and release together with transdiaphragmatic cardiac massage is attempted but is unsuccessful. At 11 transdiaphragmatic cardiac massage is discontinued. At 12 transdiaphragmatic cardiac massage together with positive inflation and negative deflation of the lung is started. This is continued to 13, where successful cardiovascular resuscitation occurs, as shown by the elevated and maintained blood pressure.

In many of these experiments, deliberate attempts were made to damage the dog's lungs by the exertion repeatedly of either maximally forceful downstrokes and/or upstrokes (pressure and suction respectively). Careful examination of the entire pulmonary tree failed to disclose any injury.

8. Courtois, M. L. H.: *Mémoire sur les asphyxies (a), avec la description d'un nouvel instrument propre à rappeler le mécanisme de la respiration*, J. de méd., chir., pharm. 82:361, 1790.

The first practical automatic suck and blow device energized by compressed gas was the pulmotor, which appeared in 1911. Booher<sup>9</sup> in 1915 demonstrated a hand-operated apparatus, called lungmotor, consisting essentially of two cylindric pumps. However, no active suction was effected by this apparatus. The E. and J.,<sup>10</sup> Emerson<sup>11</sup> and McKesson<sup>12</sup> resuscitators are gas-activated suck and blow devices of the pulmotor type.

The suck and blow apparatus utilized in my experiments is called the lungventilator. This breathing machine is operated as a hand pump.

It consists of two separate pumps, each barrel and piston unconnected with the other. One pump, or one side of the machine, is used for inflation and creates a maximum pressure of 20 mm. of mercury. The other side of the machine is used for suction deflation and creates a maximum suction of minus 10 mm. of mercury. The maximum pressure is controlled by a blow-off ball valve which vents at 20 mm. of mercury. The suction likewise is controlled as to its maximum by a valve that vents at 10 mm. This prohibits the building up of pressures greater than those quoted. That these pressures are safe is borne out by the fact that in this series of one hundred and forty-three experiments on 40 dogs no evidence of injury to the lungs was found at the autopsy of any of the animals. The safety of these pressures has repeatedly been corroborated.<sup>13</sup> The pressure and suction created by the lungventilator is conveyed, through semirigid tubing, to a Y tube immediately outside of a face mask and then into the mask itself. There is an additional safety blow-off valve in the face mask, which operates at a pressure of plus 40 mm. of mercury. Since the pressure and suction tubes are connected separately to the Y tube, either one of the tubes can be disconnected as desired, and, by alternately closing and opening the disconnected end of the Y tube, the machine can be converted and used for inflation and release or suction and release of the lung. This is a desirable added advantage.

9. Booher, J. W.: Demonstration of the Lung-Motor, *Dent. Summary* **36**: 948, 1916.

10. E. and J. Resuscitator, Inhalator, Aspirator (Fox Model) Acceptable, report of the Council on Physical Therapy, *J. A. M. A.* **121**:1219 (April 10) 1943; Footnote 2a.

11. Emerson Resuscitator Hospital and Portable Models Acceptable, report of the Council on Physical Therapy, *J. A. M. A.* **119**:414 (May 30) 1942.

12. Steinberg, B., and Deitz, A.: Manual and Mechanical Resuscitation in Experimental Asphyxia, *J. Lab. & Clin. Med.* **29**:695 (July) 1944.

13. Final Report of the Commission on Resuscitation from Carbon Monoxide Asphyxia: The Treatment of Carbon Monoxide Asphyxia, *J. Indust. Hyg.* **5**:125 (Aug.) 1923. Henderson, Y.: Resuscitation Apparatus, *J. A. M. A.* **67**:1 (July 1) 1916. Ross, B. D.: A Survey of Methods for Artificial Respiration, *ibid.* **122**: 660 (July 3) 1943. Henderson and Turner.<sup>3</sup> Coryllos.<sup>4</sup>

Two separate lungventilator resuscitators were examined and used in these experiments. The two machines are essentially similar in their construction, appearance and operation. The principal difference is that one machine has a total capacity of 600 cc. per stroke and the other machine has a total capacity of 1,000 cc. per stroke. The maximum pressure and suction are the same in the two machines. However, in the machine of 600 cc. capacity, by the removal of the steel balls in the ball valve sockets and the substitution of aluminum balls the maximum pressure is reduced from 20 to plus 10 or 12 mm. of mercury and the maximum suction is reduced from minus 10 to minus 4 to 6 mm. of mercury. This of itself does not appear to have any advantage.

In these experiments the technic was as follows:

Medium-sized dogs were anesthetized with pentobarbital sodium given intraperitoneally (1 cc. per 5 pounds [2.3 Kg.]). The femoral artery was then cannulized and connected to a recording mercury manometer which registered on a smoked drum. A small metal intrapleural cannula was then inserted into the pleural space, under air-tight conditions. This cannula was connected directly to a recording mercury manometer which registered the respirations as well as the intrapleural pressure. A close-fitting endotracheal tube with an occlusion cuff was then inserted into the trachea of the animal. After being properly placed, the occlusion cuff was then inflated, thus making the endotracheal tube completely leakproof. The mechanical resuscitator was then connected by means of a T tube to the endotracheal tube and to a recording mercury manometer which registered on the same smoked drum. Asphyxia was produced by two methods: (1) inhalation of 100 per cent nitrogen gas or (2) clamping of the endotracheal tube. The animal was asphyxiated and allowed to go to a "critical point." This "critical point" occurred in the third stage of asphyxia, with a rapidly falling blood pressure and definite changes in the rhythm and output of the heart beat. At this "critical point," various resuscitation procedures were attempted.

#### EXPERIMENTAL DATA

The chief purpose of this paper is the experimental demonstration of the importance of combining suck and blow with cardiac massage in resuscitation. A series of preliminary experiments were performed for the purpose of studying the lungventilator and to determine the value of suction and suck and blow in resuscitation. These findings differed in no essential from those demonstrated by Thompson and Birnbaum. Suffice it to say that in some experiments deliberate attempts were made to damage the lungs of the animals by exerting maximally powerful pressure and suction strokes. No injury could be demonstrated at autopsy.

#### COMMENT

The usual operating room practice in the presence of cardio-respiratory failure during a laparotomy or any other major procedure

is to inject chemical analeptics and to administer oxygen or oxygen-carbon dioxide mixtures by direct flow, i. e., positive pressure, with or without manual artificial respiration. If the experimental findings presented may be regarded as applicable to human physiology, then one must conclude that two vitally important elements are ignored in resuscitation. One is cardiac massage, and the other is the use of suction-inflation in ventilating the lungs.

Figure 1 *A* demonstrates that cardiac massage alone, massage with pulmonary suction and massage with pulmonary inflation fail to resuscitate until each is combined with suction-inflation. In figure 1 *A*, preliminary resuscitatory measures were entirely pulmonary; these failed until cardiac massage was added to suction-inflation. Figure 2 illustrates

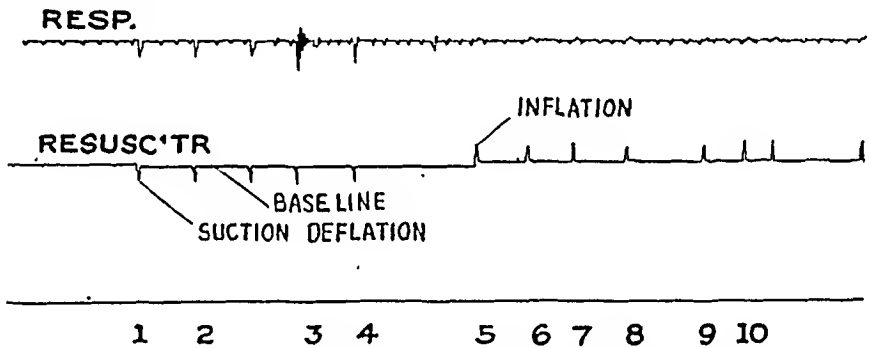


Fig. 2.—The experiment shows the effect of suction and release on the respirations of the breathing anesthetized dog and also the effect of inflation and release on the respiration of the breathing anesthetized dog. When inflation alone is used, there does not seem to be any expiratory or inspiratory stimulation and there is little or no change in the rhythm of the respiration. When suction alone is used, this causes an immediate inspiratory gasp, which is pronounced and is followed by a definite change in the rhythm of respiration.

The technic here is similar to that described in figure 1 *A*. The top line represents the respirations, and the second line represents the lungventilator. Suction was produced by use of the suction tube alone of the lungventilator, and inflation was produced by use of the inflation tube.

At 1, 2, 3 and 4 suction was produced by the apparatus. Notice that after the immediate release of suction there is an inspiratory gasp by the animal, which is decided and pronounced, particularly at 3. Notice also that there is a prolongation after each gasp, before the next inspiration occurs. At 5, 6, 7, 8, 9 and 10 inflation and release was produced. Notice that there was little respiratory effort after the release of inflation other than the normal passive expiration. There was also little or no change in the rhythm of the respiration. The inference here is that suction produces a much stronger respiratory stimulation than does inflation. This again shows the necessity of combining suction with inflation in resuscitation.

that a single suction stroke causes a reflex inspiratory gasp. Pressure strokes cause no such respiratory stimulation. In other words, while pressure alone ventilates, suction alone acts as a respiratory stimulant, i. e., a physical or reflex respiratory analeptic.

## CONCLUSIONS

1. While Coryllos and Thompson and Birnbaum have demonstrated the importance of combining cardiac massage with pulmonary ventilation in resuscitation, my experiments indicate that such a combination would frequently be inadequate if the pulmonary measures consisted in either pressure or suction used alone. The clinical implications are that suck and blow is the ventilation of choice when combined with cardiac massage.

2. In the appropriate circumstances, both cardiac and respiratory stimulation should be used in asphyxia. Either alone is often ineffective.

3. Unlike pressure, suction exerts a stimulatory effect on respiration as indicated by the inspiratory gasp caused by a suction stroke. No such effect is noted with manual artificial respiration.

## WAR WOUNDS OF ARTERIES

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**D**URING the course of one year 115 patients with arterial wounds were admitted to a general hospital in a Zone of Communications. The interval between wounding and admission to this hospital was between a few hours and three weeks. All patients had had emergency treatment and many had had definitive treatment by the time they arrived.

The following types of cases are considered in this series: (a) cases of injury to the arteries which control the main blood supply to a limb or

### *One Hundred and Fifteen Injuries to Major Arteries*

| Artery                  | Number | Gangrene | Atrophy | Arterial Operation | Gangrene Followed Injury | Aneurysmorrhaphy | Lateral Suture | Venous Graft | Exclusion Aneurysm | Simple Ligation |
|-------------------------|--------|----------|---------|--------------------|--------------------------|------------------|----------------|--------------|--------------------|-----------------|
| Carotid:                |        |          |         |                    |                          |                  |                |              |                    |                 |
| Common.....             | 4      | 0        | 2       | 2                  | 0                        | 1                | 0              | 0            | 0                  | 1               |
| Internal.....           | 4      | 0        | 4       | 1                  | 0                        | 0                | 0              | 0            | 0                  | 1               |
| External.....           | 3      | 0        | 0       | 3                  | 0                        | 0                | 0              | 0            | 0                  | 3               |
| Subclavian.....         | 1      | 0        | 0       | 1                  | 0                        | 0                | 0              | 0            | 1                  | 0               |
| Axillary and brachial.. | 51     | 10       | 6       | 11                 | 0                        | 2                | 0              | 0            | 9                  | 0               |
| Femoral.....            | 18     | 12       | 0       | 2                  | 1                        | 0                | 0              | 0            | 0                  | 2               |
| Profunda femoris.....   | 4      | 0        | 0       | 4                  | 0                        | 0                | 0              | 0            | 1*                 | 3               |
| Popliteal.....          | 30     | 22       | 4       | 3                  | 2                        | 0                | 0              | 1            | 0                  | 2               |
| Totals.....             | 115    | 44       | 16      | 27                 | 3                        | 3                | 0              | 1            | 11                 | 12              |

\* This operation required a lateral suture of the common femoral artery.

the brain; (b) cases of injury to any artery in addition to the aforementioned which resulted in gangrene, ischemic atrophy or ischemic paralysis; and (c) cases of secondary arterial hemorrhage which needed surgical intervention, regardless of the artery involved. The arteries of the forearm and lower leg below the bifurcations of the brachial and the popliteal arteries are not considered. Injury to one of them alone does not affect the circulation, and injury to all of them simultaneously is accompanied with such extensive destruction of soft tissue and bone as to amount nearly to a traumatic amputation.

The table gives a composite view of the material considered. The cases of secondary hemorrhage are not included in the table because most of them duplicate those listed in other columns.

The relative incidence of wounds of the different arteries as shown here cannot be accepted as representative of casualties as a whole. The hospital into which these patients were received was, in addition to its other duties, a neurosurgical center. The high incidence of wounds to peripheral arteries, particularly those of the upper extremity, is presumably explained by the fact that many of the patients were referred to the hospital for care of associated injuries to peripheral nerves.

#### A. OPERATION ON MAJOR ARTERIES

*I. Carotid Arteries.*—The serious import of the neurologic complications of injuries to the common and internal carotid arteries earns them special consideration. It is of note that the diagnosis of cerebral damage due to ischemia in these cases is occasionally not thought of. The most striking features that these patients present are the neurologic signs of hemiplegia and aphasia. A wound in the neck may be one of many and so may be belittled. And even if it is the only one there is a great temptation to assume at first glance that the injury to the brain is one of concussion or contusion implemented somehow or other through this wound. In 1 of our patients the diagnosis of "contrecoup injury to the brain" had been made and persisted in even though a lumbar puncture had shown "crystal clear" fluid. Makins<sup>1</sup> stated that in the first World War he heard of a craniotomy being performed in such a case.

All four injuries to the internal carotid artery were followed by hemiplegia, which persisted while the patients were in the hospital, a period of between two and three months. At the end of that time all were improving and were able to walk unattended but with a hemiplegic gait. Curiously, while these wounds were to the left internal carotid artery and all the patients were right handed, only 3 of them had aphasia. Encephalography was done on 3 patients including the patient who had no aphasia, and pronounced dilatation of the left ventricle was seen in all (fig. 1). The explanation of the absence of aphasia in the 1 case has not been made. Two of the patients showed aphonia, 1 having paralysis of the right vocal cord and the other paralysis of the left. Both of these patients arrived with tracheotomy tubes in place, made necessary by the obstruction to the airway by the paralyzed cords. In the case of the patient having the left cord paralyzed, the paralysis can, from the course of the wound, be explained only by injury to the right recurrent laryngeal nerve.

It is of interest to speculate on the nature of the arterial injury in these 4 cases. It is our impression that the circulatory deficiency was due to arterial spasm from contusion. All 4 patients presented

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1. Makins, G. H.: On Gunshot Injuries to the Blood-Vessels, Bristol, J. Wright & Company, 1919.



small penetrating or perforating wounds of the neck and little or no hematoma. In 1 of them only was there an indication for exploration (severe secondary hemorrhage from the base of the tongue). Here a segment of the internal carotid artery 1 cm. in length and about 1 cm. distal to its origin from the common carotid artery was found to be constricted to about 60 per cent of the caliber of the vessel proximal to it. The artery distal to this constriction was only slightly larger. The area was transmitting blood. The interpretation was that a



Fig. 1.—Encephalogram of a patient having unilateral internal hydrocephalus from injury to the left internal carotid artery.

contusion of the artery had caused spasm which had persisted and had become involved in scar so that it could not again attain its normal caliber. The initial acute deficiency in blood flow to the brain, possibly in conjunction with systemic shock, had been enough to cause damage to the left cerebral hemisphere. Similar conditions have been observed in other arteries, severe spasm being described at the initial operation in the forward hospital and found to be still maintained by scar tissue two months later, when exploration was done for other reasons (opera-

tion on the peripheral nerve). The 3 other cases of injury to the internal carotid artery were similar except that in all of them the course of the missile was close to the base of the skull.

Of the 4 patients with injuries to the common carotid artery, 2 suffered transient hemiplegia, which disappeared completely in a few days. In 1 of these the left common carotid artery was injured. The patient suffered aphasia, which disappeared as the hemiplegia decreased. He presented paralysis of the left vocal cord due to injury of the left recurrent laryngeal nerve. The other patient had injury to the right common carotid artery and paralysis of the right cord from damage to the recurrent laryngeal nerve on that side. The other 2 patients had arteriovenous fistulas between the common carotid artery and the internal jugular vein. In them there were no neurologic or other complications.

The nature of the arterial lesion in these injuries to the common carotid artery appeared to be more obvious than in those to the internal carotid artery. Of the 2 patients presenting transient hemiplegia, 1 had a tremendous pulsating hematoma of the neck due to a tear involving over one-half the circumference of the common carotid artery 2.5 cm. below its bifurcation. Ligation of the artery was performed four days after wounding and one day after admission to this hospital. The ligation apparently did not arrest the recovery of the hemiplegia. The other had a traumatic aneurysm, 3 by 5 cm., just above the sternoclavicular joint on the right. A septic pulmonary infarction and empyema developed, and the patient was evacuated, two and one-half months after being wounded, to the United States for further treatment. One of the 2 patients without hemiplegia had a small arteriovenous fistula of the right common carotid artery and the internal jugular vein. Aneurysmorrhaphy was performed. The result was good, and the patient was discharged to duty. The other presented a larger arteriovenous aneurysm, a severe wound with loss of tissue of the face and mandible, and was evacuated for later elective operation.

The testimony of this small group of cases confirms the common teaching that injury to the internal carotid artery is more serious than that to the common carotid artery so far as the resultant damage to cerebral tissue is concerned. The syndrome with hemiplegia, no hematoma in the neck, fracture of the mandible, injury to the vagus nerve or its branches (laryngeal paralysis), injury to the cervical portion of the sympathetic system (Horner's syndrome), clear spinal fluid and normal roentgenograms of the cranial vault suggests injury to the internal carotid artery. An injury to the common carotid artery is perhaps distinguished from this by the commoner occurrence

of pulsating hematoma, Horner's syndrome and injury to the vagus nerve and by the comparative rarity of mandibular fractures and hemiplegia.

*II. Subclavian Artery.*—Only 1 patient was admitted with injury to the subclavian artery. There was an associated partial paralysis of all cords of the brachial plexus. The arterial lesion was a traumatic aneurysm (6 by 10 cm.) from a wound of the second portion of the artery. This was excised after ligation of the first and third portions of the artery and ligation of the subclavian vein. A neurolysis of the brachial plexus was performed. The clavicle was resected in its middle third to accomplish this. There was no change in the circulation of the hand following operation other than that the radial pulse diminished but did not disappear. A dorsal sympathectomy had been done nine days prior to the attack on the aneurysm. This caused to disappear a considerable degree of causalgia which had previously been present.

The interest in the subclavian artery centers around the technic of an operation which in World War I was supposed to carry a prohibitive mortality. The danger then was recognized to be from hemorrhage and shock, not from gangrene. Our impression is that the ligation of the subclavian artery is technically as easy as that of any other artery provided four things are insisted on: (1) adequate exposure, (2) good anesthesia given intratracheally, (3) blood transfusion and (4) patience to operate for from four to six hours if necessary. During World War I the first point was the only one stressed, chiefly because points 2 and 3, on which point 4 depends, were not available, as they are now. The angular incision of Fiolle and Delmas<sup>2</sup> with resection of the clavicle, particularly on the left side, where the vessels are more inferior, should be routine.

*III. Axillary and Brachial Arteries.*—There were forty-one injuries to the brachial artery and ten to the axillary artery. The dividing line between these two arteries is the outer border of the teres major,<sup>3</sup> and classically this point is distal to the anterior and posterior circumflex humeral branches. The branches of the axillary and brachial arteries are well known to be subject to such an infinite variety of anomalies, however, that any nominal distinction between the two arteries as to which is the most dangerous to tie is rendered unimportant. Even the consideration as to whether the ligation is done above or below the profunda brachii is of little significance if one compares it with the importance of the intact collateral circulation, frequently a doubtful factor in large traumatic

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2. Fiolle, J., and Delmas, J.: *The Surgical Exposure of the Deep-Seated Blood-Vessels*, London, William Heinemann, Ltd., 1921.

3. Gray, H.: *Anatomy of the Human Body*, ed: 22, Philadelphia, Lea & Febiger, 1930, p. 587.

wounds of the arm. It is my experience that ligation of the brachial or axillary artery above or below the profunda brachii in a young patient with intact collateral vessels is completely safe.

The frequency of associated injury to the nerve is evident when it is realized that of the 41 patients with injury to axillary or brachial arteries who did not have such extensive gangrene that they could be examined for neural injury, only 1 did not have an accompanying neural lesion. There were 49 patients admitted to the hospital during this period who had injuries to the brachial plexus without vascular injury which could be detected clinically or appeared in the record. About 50 per cent, then, of injuries to the brachial plexus are accompanied by injuries to the axillary or brachial artery, whereas almost 100 per cent of injuries to these arteries have associated injury to nerves.

Operation on the axillary or brachial artery was performed in this hospital on 11 patients. Ligation of the artery was performed in 9 cases, and endoaneurysmorrhaphy was done in 2. In 1 of the cases of endoaneurysmorrhaphy the radial pulse persisted normally postoperatively; in the other it did not. Normal circulation in the hands was preserved in both. Of the patients having ligature of the artery, in some a weak palpable radial pulse was preserved, in some the pulse disappeared and in others there was no pulse prior to operation. The level of the ligation (i. e., above or below the profunda brachii artery) apparently had no bearing on this.

In the technic of operation on these two arteries, there are several points that are worth emphasizing. Exposure is, as in all arteries, the most important. The pectoralis major and minor should be divided in any patient who has a wound to the artery that is higher than midarm. This is particularly true if there is an aneurysm or a pulsating hematoma and certainly will have to be done if there is a divided nerve in this region that will need suturing. In a patient with aneurysm or pulsating hematoma whose wound is so proximal that a tourniquet cannot be applied above it, the preliminary dissection should be most careful and prolonged. Two or three hours may be necessary in order to get well behind the lesion and around it on as many sides as possible before it is broken into. This is important because the hemorrhage caused by breaking into the aneurysm can always be easily controlled if the operator is in a position to lift the whole neurovascular bundle forward with the fingers, thereby applying enough tension to stop bleeding and allow careful dissection of the lesion (fig. 2). In all cases a provisional ligature of tape tied down over a rubber tube in order to protect the wall of the vessel from the trauma of the knot<sup>4</sup> is placed on the main artery at the nearest spot to the aneurysm that is easily

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4. Watson, G., cited by Makins.<sup>1</sup>

accessible. One of the most difficult features to deal with in dissecting out lesions of the brachial and axillary arteries is hemorrhage from the venae comitantes and their branches, which communicate across in front of the artery. These are often involved in scar and have thin walls. If they cannot always be dealt with by ordinary dissection, they can be secured with the neurovascular bundle on tension as described in the dissection of the artery.

The great majority of our patients were received with limbs in plaster casts. This included some patients who had no fractures and who had been immobilized presumably to protect their large wounds according to the teachings of Trueta.<sup>5</sup> Two of these were definitely felt to have been harmed by this procedure, 1 having an amputation

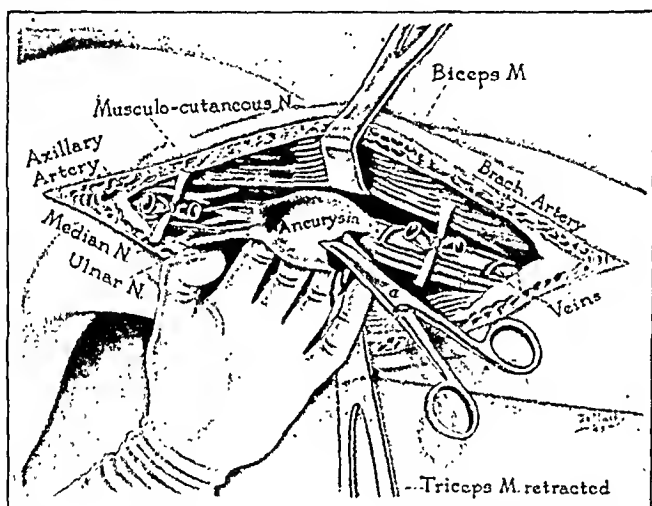


Fig. 2.—Diagrammatic representation of the technic of approach to an aneurysm of the brachial artery. Note Watson's temporary ligatures in place on the artery.

through the forearm at a higher level than had been expected before the limb had been put in plaster and the other receiving a stiff and edematous hand, with some areas of pressure necrosis beneath the cast. It is our conviction that, regardless of fractures, no patient who has had ligature of a main artery of a limb should be placed in a circular bandage of any kind, least of all a plaster cast, until the circulation of the limb has become stabilized at the level which it is finally going to attain. This means that if the patient has no gangrene he shall be kept free for a period sufficient to insure that no gangrene will ensue (at least three days) and that if he does have gangrene he be kept free either

5. Trueta, J.: *Treatment of War Wounds and Fractures with Special Reference to the Closed Method as Used in the War in Spain*, New York, Paul B. Hoeber, Inc., 1940.

until the gangrene is completely dry, with no surrounding edema, or until amputation is done.

Varying degrees of causalgia were frequent in this group. It is difficult to recall a patient with aneurysm or pulsating hematoma that did not suffer this symptom. This could be relieved by dorsal sympathetic block for short periods or, as in the case with the subclavian aneurysm, by dorsal sympathectomy, but the excision of the aneurysm and lysis or suture of the involved nerves were most successful.

The great importance of physical therapy in the treatment of these wounds of the arm has been impressed on us. If there has been any ischemic myositis or paralysis, much can be gained by active and passive motion if they are started early. The presence of dry gangrene is no contraindication to this. In many cases nerves that were thought to be completely paralyzed recovered function in a surprising manner after they had responded to this treatment.

*IV. Femoral Artery.*—There were 18 patients. Eight of them arrived with amputation already performed, and because of inadequate records as to the level of the arterial injury the cases are not of much value for study. Three patients had amputation below the knee, and the other 5 had amputation above. Of the 10 who arrived without amputation, 6 had had the continuity of the femoral artery interrupted prior to admission. Of these, 2 had gangrenous legs and had amputation at this hospital; 4 had limbs with adequate circulation. The remaining 4, who arrived without amputation, were patients who suffered injury to their femoral arteries without interruption of arterial flow through the area. Two of these had aneurysms which were not operated on in our hospital. A third had an enlarging hematoma requiring ligation of the artery, a lumbar sympathectomy being performed four hours later. The case of the fourth patient was a puzzling and tragic one. Ligation of the profunda femoris artery was necessary because of secondary hemorrhage from severe wounds of the thigh. Further secondary hemorrhage then resulted from the main trunk of the femoral artery which had been seen to be intact at the original operation. It was necessary to ligate the femoral artery in the midst of infection, and the leg was lost, the patient dying subsequently of overwhelming infection due to *Klebsiella pneumoniae*. The case was of interest in the light of a similar one at another hospital, in which rupture of a previously intact common femoral artery occurred a few days following ligation of the femoral vein. Why a normal main femoral artery should become involved in the process and bleed in both instances has not yet been explained.

Of the four amputations for femoral artery injury performed in this hospital, two were done below the knee and two above. The two

that were done above were extremely high, a subtrochanteric and a hip joint disarticulation.

The related experience has given us a great respect for the common femoral artery. It must be borne in mind, however, that all the ligations performed were in nonelective cases. We have no data on the incidence of gangrene following elective ligation.

*V. Profunda Femoris Artery.*—There were four lesions of the profunda femoris artery and its branches. One was an arteriovenous aneurysm arising within 1 cm. of the origin of the profunda from the common femoral artery and causing an aneurysmal sac of a dumbbell shape involving the profunda femoris vein and the superficial circumflex iliac vein. This was excised so close to the common femoral artery that a lateral suture of it had to be performed. The other three were secondary hemorrhages from the profunda femoris or its branches in association with subtrochanteric fractures of the neck of the femur. One ligation was done elsewhere; the other two were done here. These patients presented special problems because it was necessary to find the bleeding point, amidst a large amount of callus and damaged muscle, usually after the patient had stopped bleeding. In both patients this took several attempts, with the inevitable result that infection and osteomyelitis ensued. In 1 case this was not serious, but in the other, the 1 in which the common femoral artery gave away after the ligation of the profunda, it meant loss of the leg and, later, loss of the patient's life.

The lesson to be learned from these cases is that when one is presented with secondary arterial hemorrhage from the region of a subtrochanteric fracture of the femur one should prepare for an extensive operation, ligate the profunda femoris artery above the origin of the femoral circumflex branches and then open the whole region of the fracture and secure the bleeding point for sure at the first attempt. The common femoral artery should be disturbed as little as possible during this procedure.

*VI. Popliteal Artery.*—There were 30 patients with injuries to the popliteal artery. Of these, 22 had gangrene of such an extent that in all but 1 amputation was performed. Four others had atrophy, Volkmann's contracture or ischemic myositis, whatever term one wishes to use. Ten of the 21 who came to amputation had no associated fracture; the other 11 did.

Of the 3 patients who underwent arterial operation at this hospital, gangrene developed in 2 and required later amputation. One of these, a patient who had a near traumatic amputation of his leg in an automobile accident, was received shortly after his accident. His collateral circulation had been completely destroyed by the trauma. A venous graft was attempted but was given up because of technical difficulties arising from

severe damage to the artery over a long area. Amputation was done forty-eight hours later. The other was a battle casualty that had a pulsating hematoma of the popliteal space from a wound of the artery two and a half weeks previously. The hematoma increased in size and eventually dissected almost up to the femoral triangle. Surgical intervention became necessary. There was no back bleeding from the artery at the time of ligation, and during the four hours following it it became obvious that the leg was not going to survive. The wound was therefore reopened, a venous graft sewed in place and the patient immediately heparinized. Although the graft was functioning at the close of procedure and heparinization was continued, the leg became gangrenous and was amputated. Later examination of the artery showed that the graft had become solidly clotted. The third patient, the 1 who did not get gangrene, underwent excision of a popliteal aneurysm one week after lumbar sympathectomy. He did well. There was no question about the viability of his foot at any time following operation.

Supracondylar fractures of the femur with contusion or rupture of the popliteal artery present a special problem because of the severe damage to collateral vessels as well as to the main artery. Of 4 such cases in our series, amputation was done in all and the circulatory damage was so severe that in only 1 of the patients could the knee joint be preserved. In that patient the stump left was only 5 cm. long, measuring from the tibial tubercle.

Of the twenty-one amputations for injury to the popliteal artery, eleven were performed above the knee joint and ten below. In these ten, six of the stumps were so short as not to be of much value for a prosthesis. Of the 4 patients having good length in their below knee stumps 2 had had lesions which had not entailed rupture of the artery but rather, thrombosis or spasm. The other 2 had suffered rupture of the artery with hemorrhage into the popliteal space but had had extensive surgical incisions made through the fascia, enabling evacuation of the clot. The patients who underwent amputation close below the knee or above it did not have extensive incisions of this nature. It appears that these incisions to relieve pressure on collateral vessels are decidedly advantageous. Closed as well as open fractures of the lower femur or upper tibia and dislocations of the knee joint which have any evidence of damage to the popliteal artery should have exploratory incisions made in the popliteal space and the incisions left open if there is any evidence of hematoma or swelling.

#### B. SECONDARY HEMORRHAGE

There were 13 cases in which secondary hemorrhage was severe enough to require operative intervention or to cause death. There were



many other cases of minor hemorrhage which required only packing and of which no records were kept. There were over 9,500 casualties treated during this time. The figure of 13 was far lower than one would have predicted out of this total number.

The ligations that were done for hemorrhage were of the following arteries: common femoral, one; superficial femoral, one; deep femoral, two; popliteal, one; posterior tibial, one; brachial, one; external carotid and common carotid combined, one; external carotid alone, two; internal pudendal, one, and right lumbar, one.

The patients who suffered loss of a leg following treatment of secondary hemorrhage from the popliteal, deep femoral and common femoral arteries have been mentioned. Other interesting special problems and situations were encountered as enumerated in the following paragraphs.

One patient who had a severe secondary hemorrhage from a wound which perforated the cecum and injured a right lumbar vessel required a diversion of the intestinal stream from the area by an ileotransverse colostomy before the bleeding was satisfactorily controlled.

One patient who had suffered a gunshot wound of the neck died suddenly from rupture of a traumatic aneurysm of the superior thyroid artery into the larynx, a lesion which had previously been in no way suspected.

One patient had twelve secondary hemorrhages from his mouth following a penetrating oblique wound from a shell traversing the submental region, shattering his right mandible and causing aphasia and right hemiplegia from contusion of the left internal carotid artery. Although three of these hemorrhages were so severe as to result in almost complete exsanguination, their source, which turned out to be a branch of the left lingual artery presenting in the pharynx 2 cm. posterior to the fauces, was not found until the pharynx was examined with the patient under general anesthesia. Prior to this the opinion was that the bleeding was coming from the shattered right mandible, since complete visualization of the posterior pharynx was not possible, due to trismus.

Another patient suffered a gushing hemorrhage from a small aneurysm of the internal maxillary artery presenting below the inferior turbinate in the left naris. This would have been rapidly fatal had not the Chief of the Section of Otorhinolaryngology, Capt. A. C. Johnson, been in the ward at the time of the occurrence to insert a packing. He ligated the external carotid artery immediately and later injected sclerosing solution into the area. Many weeks later the aneurysm was seen to be in a much collapsed state.

In general our impressions with regard to secondary hemorrhage are that: (a) if a main artery of a limb must be ligated as an emergency

measure for hemorrhage the limb stands a much poorer chance of survival than if the ligation can be done as an elective procedure; (b) hemorrhages from traumatic lesions of arteries lying in or beneath mucous membranes are particularly perilous, and (c) if the hemorrhage is going to be attacked surgically this should be done radically and completely at the first operation.

### C. COMMENT

I. The critical arteries are the popliteal, the internal carotid and the common femoral. Others become critical if the collateral circulation has been injured by the wound. This must always be taken into account when a case is evaluated.

II. The place of sympathectomy or repeated anesthesia of the sympathetic chain is not easy to evaluate. It is our definite impression, however, that the chief time for sympathectomy is prior to operative interruption of a critical artery. Its use as a prophylactic against spasm of collateral arterial supply is its most important function. If there is not time to do it before and it can be performed within six hours after such interruption, it is also worth doing but much less benefit can be expected therefrom. The one exception to this occurs in the event that the arterial lesion at the time of the débridement has been shown to be one of spasm, as occurred in one injury to the popliteal artery that we observed subsequent to this group. Sympathectomy is then the treatment of choice at any time.

Procaine hydrochloride injected paravertebrally should be used in cases of arterial wounds only in which the condition of the patient does not warrant the operation of sympathectomy, and the injections should be repeated intermittently as frequently as practicable for as long as a favorable response is obtained. This usually will not be longer than forty-eight hours after injury.

These recommendations sound radical, but they in fact advocate meddling with the sympathetic systems of fewer patients than has been the general custom. The patient in whom procaine hydrochloride injected paravertebrally is to our mind of little value is the familiar one who is seen a day or two after injury and in whom ischemic demarcation has already started. We have observed little benefit either from the standpoint of saving the limb or from that of lowering the level of demarcation by the use of procaine hydrochloride injected paravertebrally or of sympathectomy in these cases.

III. The pattern of gangrene in limbs with injuries to critical arteries is a subject on which much interesting work is still to be done. The fact that in all such patients the skin is viable well below the level of dead muscle is a common observation. Extreme examples of this

have occurred when 2 patients with injury to the popliteal and brachial arteries respectively presented external evidence of gangrene of only the tips of the fingers and toes. As time passed, liquefaction of all the muscles of the calf in 1 case and those of the forearm in the other supervened, without further cutaneous gangrene.

The interesting anatomic observations of Clark and Blomfield,<sup>6</sup> which divide muscles into various groups based on the pattern of the arterial circulation within them, demonstrate that the gastrocnemius and soleus muscles possess a far poorer potential collateral circulation than the deeper muscles of the leg. It has in general been our experience that these two muscles show gangrene to a higher level than the deeper ones. The importance of doing selective débridement of these muscles at the time of amputation is evident.

·IV. The importance of a test or sign which would enable surgeons to tell preoperatively whether ligation of a given artery will result in gangrene is obvious. The practical importance of such a test would be that it would tell whether it is necessary to attempt an anastomosis or venous graft or whether simple ligation is safe. We have used the Henle-Coenen test.<sup>7</sup> This consists in consideration of the briskness of the blood flow from the distal cut end of the artery as observed on the operating table as an indication of the amount of arterial pressure and blood flow being brought into the distal limb by the collateral vessels. In no case in which we have ligated an artery using this sign as an indication has any trouble ensued. In 1 case the complete lack of back bleeding from the distal cut stump of a popliteal artery prompted us to sew in a venous graft. The graft unfortunately failed, and gangrene ensued, showing that one's fears based solely on this sign were well founded. Our experience with emergency ligations has been limited, however, and personal communications from surgeons in forward hospitals who have been intimately associated with the emergency cases say that this sign has been unreliable. The state of the vessels of the limb is at that time in a transitory stage. The amount of spasm and thrombosis of the collateral vessels which will eventually be present has not yet become established. This consideration apparently may invalidate any early decision that is made. For the late elective case, however, in which these factors are stabilized, the sign in the opinion of my colleagues and me is a valuable one.

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6. Clark, W. E. L., and Blomfield, L. B.: The Efficiency of Intramuscular Anastomosis with Observations on the Regeneration of Devascularized Muscle, *J. Anat.* **79**:15 (Jan.) 1945.

7. Matas, R.: Testing the Efficiency of the Collateral Circulation as a Preliminary to the Occlusion of the Great Surgical Arteries, *J. A. M. A.* **68**: 1441 (Oct. 24) 1914.

## SUMMARY

The following are the most important lessons and impressions that have been learned from the experiences related.

1. The critical arteries are the popliteal, the internal carotid and the common femoral. Others become critical if the collateral circulation has been involved in the wound.

2. Early ligation or ligation for secondary hemorrhage is dangerous. Late or elective ligation is much less so.

3. Sympathectomy should be done if possible before or immediately after ligation of critical arteries. If impossible, sympathetic blocks should be used for forty-eight hours.

4. The release from closed spaces, such as the popliteal space, of blood clot or edema through large incisions which are left open is of extreme importance in the affording of free flow through collateral vessels. The particular application of this procedure to patients with supracondylar fractures of the femur is emphasized.

5. In early cases of wounds of critical arteries the use of venous grafts or prostheses is indicated.

6. In the decision as to whether a graft or prosthesis should be used in a patient having a late or elective ligation, lack of good arterial back bleeding from the distal stump is the one most important indication for their use.

7. In operations on hematomas or aneurysms, long incisions, wide dissection (preserving as much collateral circulation as possible in the process) and provisional ligatures with tape over a rubber tube are recommended.

8. A circular bandage should not be used in any limb that has doubtful circulation. Patients with such limbs should not be moved from the hospital where they were first admitted until the circulation is stabilized.

Major Charles L. Neill and Capt. Ludwig H. Segerberg, of the Section of Neurosurgery, allowed me to include the neurologic cases in this series.

## GLOMUS TUMORS (ANGIONEUROMYOMAS)

A Clinical and Pathologic Report of an Unusual Case

HARRY JACKSON, M.D.

AND

RUTH BALKIN, M.D.

CHICAGO

IT HAS long been taught that the dilatation and contraction of the capillaries of the skin helps to regulate the heat of the body. That there is an accessory vascular apparatus called the glomus also present is not so generally appreciated.

### HISTORICAL DATA

In 1920, Barré, a French surgeon, removed a tiny painful tumor from beneath a finger nail and gave it to P. Masson for pathologic study. In his report of this tumor in 1924<sup>1</sup> Masson gave to the world the first description of a neoplasm originating in a glomus. It was bluish red and 3 to 4 mm. in diameter and was composed of large, clear, round or polyhedral cells, which were similar to those found in the coccygeal gland or glomus. Besides these "epithelioid" cells, there were present in the tumor mass arterioles, veins, smooth muscle cells and nerve fibers. Masson was so struck by this conglomeration of epithelioid cells, blood vessels, nerves and muscle that he combed the anatomic atlases for a possible explanation. He found that Sucquet<sup>2</sup> in 1862 first described peculiar arterioles in the palms and soles which opened directly into neighboring veins, without forming a capillary network. Further search revealed that H. Hoyer<sup>3</sup> had given a more detailed description of an arteriovenous anastomosis in the skin of adults. This anastomosis takes the form of a coiled arteriovenous mechanism, which Masson named the Sucquet-Hoyer canal. Masson was forced to the conclusion that Barré's tumor was an organoid overgrowth of all the elements that go to make up the glomus entity. He thus was the first investigator to describe this tumor and to explain the anatomic and physiologic implications of it.

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Read before the Chicago Surgical Society Dec. 7, 1945.

1. Masson, P.: *Le glomus neuromyo-artériel des régions tactiles et ses tumeurs*, Lyon chir. **21**:257 (May-June) 1924.

2. Sucquet, cited by Testut, J. L.: *Traité d'anatomie humaine*, Paris, O. Doin, 1921, vol. 2, p. 101.

3. Hoyer, H.: *Ueber unmittelbare Einmündung kleinster Arterien in Gefäß-äste venösen Characters*, Arch. f. mikr. Anat. **13**:603, 1877.

Ten years later, Nicholas W. Popoff,<sup>4</sup> of Rochester, N. Y., published a paper entitled "The Digital Vascular System." Popoff had been impressed by the increasing number of painful tumors of the skin of the extremities that had been reported since Masson's report in 1924, and he decided to make a detailed anatomic study of the skin of the digits. He was rewarded in his search by the finding of large numbers of a normal anatomic entity, the glomus, consisting of an afferent artery which breaks into a coiled arterial organ—the Sucquet-Hoyer canal. Furthermore, he found preglomic arterioles, with clear periglomic expansion zones, furnished with neuroreticular mechanisms of sympathetic and myelinated nerves, which control the Sucquet-Hoyer canal. The glomus also has a specially arranged system of collecting veins and an outer lamellated collagenous zone surrounding the entire glomus. By this mechanism, a large amount of blood can quickly be shunted into the skin to help regulate the general or local temperature of the body. Popoff found most of these glomus units on the digits and in the palms and soles. Large numbers, however, were also present in the skin of the extremities and lesser numbers on the trunks of adults. He found none in infants, a fact which explains their inability to accommodate themselves to sudden changes of temperature. Glomus units have been found in all warm-blooded animals.

The first glomus tumor to be reported in this country was seen by Mason and Weil<sup>5</sup> in 1934. Since that time, some three hundred glomus tumors have been collected from the literature. Before they were classified as glomus, the older clinicians knew them as painful cutaneous tubercles. O. T. Bailey,<sup>6</sup> writing in "Oxford Medicine" in 1939, collected 100 cases and gave the tumor the title of glomangioma. The *Quarterly Cumulative Index Medicus* of the American Medical Association classes them as angioneuromyomas. Beaton and Davis reported 3 cases in 1941 and collected 271 cases from the literature.<sup>7</sup>

#### ETIOLOGY

There is no known etiologic factor; trauma has not been found to be a cause. The two sexes are attacked equally, and no race is immune.

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4. Popoff, N. W.: Digital Vascular System, with Reference to State of Glomus in Inflammation, Arteriosclerotic Gangrene, Diabetic Gangrene, Thromboangiitis Obliterans and Supernumerary Digits in Man, *Arch. Path.* **18**:295 (Sept.) 1934.

5. Mason, M. L., and Weil, A.: Tumor of Subcutaneous Glomus, *Surg., Gynec. & Obst.* **58**:807 (May) 1934.

6. Bailey, O. T., in Christian, H. A.: *Oxford Medicine*, New York, Oxford University Press, 1939.

7. Beaton, L. E., and Davis, L.: Glomus Tumor: Report of Three Cases, *Quart. Bull., Northwestern Univ. M. School* **15**:245, 1941.

## SYMPTOMS

The tumors are usually small, ranging from 2 to 5 mm. in diameter. Some have reached 3 cm. in diameter. They are of firm consistency and limited growth. They are usually blue or red, the degree of color depending on the size or depth of the tumor. They are well circumscribed and movable when in the cutaneous tissues, where they are superficial to the superficial fascia. Many are found beneath the nails of the fingers or toes, where they produce excruciating pain, which often radiates up the arm to the face or along the leg for long distances. The pain is often lancinating or stabbing or pulsing in character and is activated by contact with the outer clothing or changes in temperature, or it may occur spontaneously. Pulsative tumors may erode bone when in contact. Atrophy of muscle may be associated but is usually a phenomenon of disuse of the part due to the pain. When the tumor is subungual, the nail may be curved and thickened, with longitudinal striations. The nails are often left uncut because of the severe pain. When excised completely, the lesions usually do not recur. Pain usually ceases after removal of the tumor, but sometimes it persists for a time. The tumor usually occurs singly, but it may be multiple; as many as forty-eight have been found in 1 person. Two-thirds of the reported tumors have been located on the upper extremities.

The tumors appear early in middle life and may be present for several years before the patient seeks relief of the pain or discomfort.

## DIAGNOSIS

The firm, circumscribed, superficial nodules, bluish or red, the presence of pain out of all proportion to the size of the tumor and the demonstration by microscopic section of the presence of layers of large epithelioid glomus cells with myelin and nonmyelin nerve fibers in direct continuity with the cytoplasm are pathognomonic.

## DIFFERENTIAL DIAGNOSIS

The true glomus tumor must be differentiated from most benign tumors of the skin such as fibroma, angioma and angiomatous leiomyoma. The malignant sarcomas, melanoblastomas and carcinomas are easily differentiated by their more rapid growth and microscopic characteristics. Felon, subungual exostosis or periostitis and subungual wart may produce pain.

## TREATMENT

Complete excision usually cures. In the nail bed, the nail must be excised over the tumor to allow a complete excision. In the skin the mass is easily excised from the surrounding subcutaneous tissue, with the patient under local anesthesia.

## REPORT OF A CASE

A Negro coachman and houseman, 68 years old, first noticed a small nodule in the skin of the flexor surface of the left forearm, just below the elbow, twenty-five years before he consulted us. It grew slowly and did not cause appreciable pain until about five years later. For the past two years the pain, beating in character, has become more insistent and has awakened him from sleep. For the past year it has interfered with the use of the arm.

On examination, the mass is slightly movable over the brachioradialis muscle, in which it has caused a depression. The skin is attached but not discolored. The mass is about 4 cm. in diameter and slightly sensitive to manipulation. The largest tumor of this type heretofore reported has measured 3 cm.

Results of the general examination of the patient were negative as was also the reaction to the Wassermann test. Past history is noncontributory except for this new growth. The patient asks that the tumor be removed on account of the pain, spontaneous and throbbing but not radiating, which has now become unbearable.



Photomicrograph showing layers of epithelioid cells and dilated vascular channels.

*Treatment.*—With the patient under local anesthesia the mass was excised from the surrounding fatty subcutaneous tissue, and healing took place uneventfully.

*Pathology.*—The specimen consists of a well encapsulated tumor that measures 4 by 2.5 by 2 cm. It is moderately firm, and the sectioned surface is deep red and has a spongy appearance.

Microscopic section of the tumor reveals it to be encased in a dense hyaline connective tissue capsule. The tumor itself is composed of numerous vascular channels which are the size of dilated capillaries, such as are seen in capillary hemangiomas. These channels have walls that consist of a single layer of endothelium and are surrounded by cords and sheets of cells which are round to oval in shape and regular in size and have poorly defined cell membranes. In some areas these cells are rather closely packed together, but in other zones they are more widely spaced. However, in both areas an eosinophilic fibrillar network can be seen between the cells. Occasional short, thin strands of smooth muscle can be seen in the tumor as well as small thick-walled arteries, which are most numerous at the periphery.



## DISCUSSION

DR. HILLIER DAVIS: A patient operated on by me at the Cook County Hospital several years ago showed a mass in the omentum and multiple tumors of the intestine, which bled readily when touched.

DR. RUTH BALKIN: Dr. R. Jaffe performed an autopsy on this patient and found a primary tumor of the omentum, with metastases throughout the abdomen. The tumor had all the characteristics of a glomus, and in his opinion this was a unique case, as no malignant growth of this type had ever been reported up to that time and there have been none reported since.

## MIGRATORY POLYPHLEBITIS

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**M**OUNTING interest in peripheral vascular diseases is evident from the large volume of literature on this subject in textbooks and current surgical journals. However, one type of structural vascular disease infrequently discussed is migrating phlebitis.

This type of phlebitis is a primary inflammatory lesion of a venous segment with secondary vasomotor disturbances. Characteristically, it involves a segment of vein and subsides in the original area only to appear in another segment of vein in the same or opposite leg. Because of this tendency it is my preference to term this entity migratory polyphlebitis.

Polyphlebitis of this type usually involves the surface veins of the legs. However, it may occur in the deeper veins. The upper extremities may become the site of this disease as well as the lower extremities. I have seen vessels of the anterior part of the abdominal wall involved with this process.

### ETIOLOGY

Migratory polyphlebitis when not associated with thromboangiitis obliterans (Buerger's disease) should be considered as a forerunner of this disease. Thus the etiology falls into the same category as that of thromboangiitis obliterans. However, migratory polyphlebitis is not confined to the Jewish race, nor does it have a high incidence in this race, as does thromboangiitis obliterans. The 4 patients under present discussion were all male patients, none of whom were Jewish. Migratory polyphlebitis occurs almost always in men. This fact has led some investigators to state the belief that estrogenic hormones are beneficial as a therapeutic measure in the treatment of this disease.<sup>1</sup> Usually the disease is seen in young adults, between 20 and 40 years of age. Some authors have expressed the opinion that there is a familial trait or tendency toward thromboangiitis obliterans, and this may also be applied to migratory polyphlebitis.<sup>2</sup> In view of the inflammatory reaction of this disease process, many investigators have cultured

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From the surgical service of Dr. John F. Raycroft, Kings County Hospital.

1. McGrath, E. J.: *Experimental Peripheral Gangrene*, J. A. M. A. **105**:854 (Sept. 14) 1935.

2. Collens, W. S., and Wilensky, N. D.: *Peripheral Vascular Diseases*, Springfield, Ill., Charles C Thomas, Publisher, 1939.

various types of bacteria.<sup>3</sup> The role of tobacco has been accentuated as being deleterious to all types of patients with peripheral vascular diseases. The basis for this is the knowledge of the profound spasm of peripheral vessels which occurs in the presence of nicotine. However, it is doubted that there is a causal etiologic relationship between tobacco and inflammatory lesions of blood vessels. Once the disease has occurred, tobacco should be considered as definitely deleterious.

In a discussion of the etiology of this disease, mention should be made of the fact that in my experience almost all patients with migratory polyphlebitis present a significant antecedent history. The historical data may be those of trauma to the extremities, frostbite or an acute systemic febrile disease such as pneumonia. Although these factors do not precipitate an acute episode of polyphlebitis, they may be initiating factors in the production of the disease in a patient with an underlying tendency toward peripheral vascular impairment.

#### PATHOLOGY

Migratory polyphlebitis is an inflammatory lesion. It is a primary structural vascular disease which may cause secondary vasomotor disturbances. This disease is characterized by the fact that it involves venous segments and recedes in the original area only to commence in a segment of vein elsewhere. Its migratory tendency is similar to that of migratory polyarthritis in acute rheumatic fever. This is significant because a segmental occlusion of a major vessel does not necessarily interfere with the collateral circulatory function.

During the acute phase of polyphlebitis the superficial veins are affected. The involved segment is acutely inflamed, reddened and tender to palpation. The condition in an involved segment will run a course from seven to fourteen days. Subsidence of the acute infection results in a hard vein similar to a goose quill. Pigmentation occurs about the segment. With the onset of pigmentation, another venous segment may become involved. Early lesions are confined to veins alone. However, as the disease progresses, the arteries may become involved. Careful interrogation of patients with full-blown thromboangiitis obliterans will often elicit a history of migratory polyphlebitis. It may, therefore, be considered a forerunner or a manifestation of thromboangiitis obliterans.

#### CLINICAL PICTURE

The patient is usually a young man. The significant physical findings are revealed in the area of complaint. This is usually a venous segment of the leg which presents the physical characteristics previously

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3. Allen, E. V., and Lauderdale, T. L.: Accidental Transmission of Thromboangiitis Obliterans from Man to Man, *Proc. Staff Meet., Mayo Clin.* **11**:641, 1936.  
Goodman, C.: A Skin Test to Suggest the Diagnosis of Typhus and Thromboangiitis Obliterans, *Bull. New York Acad. Med.* **11**:403, 1935.

mentioned. The lesion is fundamentally an acute inflammatory process without systemic response to an inflammatory reaction such as chills or fever. When migratory polyphlebitis involves the deeper veins, the diagnosis is most difficult, since there is no redness, tenderness or other evidence of acute inflammation. However, deep vascular involvement in the leg may produce a positive Homan sign, cramps or edema resulting from venous obstruction. Edema of this type is identified by the rapidity with which it appears.

The following cases have come under my personal observation during the past three years. Each presents a most interesting lesson in migratory polyphlebitis.

CASE 1.—The patient, Frank W., aged 24, was seen Dec. 1, 1943, at which time he presented a history of having had pleurisy and pneumonia in 1940. One year later he noticed reddened areas over the veins of his legs, which would last about two weeks and disappear only to appear elsewhere. This process continued intermittently for about a year. He visited his doctor, who advised and performed a bilateral ligation high in the saphenous vein. Shortly thereafter slight edema of both legs developed. In December 1943 he entered Kings County Hospital because of the presence of reddened veins in the anterior part of the abdominal wall which were similar to those which had developed previously in his legs. A biopsy was performed, a portion of the vessels of the anterior part of the abdominal wall being excised, and was reported to show thromboangiitis obliterans. The patient was treated conservatively. He was sent to a home for convalescents in the upper part of New York state. On March 10, 1944 signs of an acute condition within the abdomen developed. He was operated on, and the following significant conditions were unfolded: (1) superior mesenteric thrombosis, (2) thrombosis of the portal and hepatic veins and (3) acute gangrenous appendicitis with thrombosis of the appendical vessels. The patient died shortly after operation.

CASE 2.—The patient, William T., aged 19, was seen in consultation on Jan. 21, 1946. The history is one of fifteen months' duration. His first complaint occurred at the time when reddened, indurated areas developed about his left ankle, which disappeared only to appear about his left knee several weeks later. After this episode, he had a similar experience with the development of reddened areas above the left knee. During these fifteen months he had sporadic episodes of edema of the left ankle. Three days prior to his present examination he noticed two reddened areas on the medial aspect of his right tibia. He had no systemic reaction such as chills or fever during any part of the fifteen month period. Examination was essentially noncontributory excepting for the pertinent findings in the lower extremities. Both legs were grossly symmetric in size, shape and development. Bilateral pulsations of the major vessels were demonstrated. There was no alteration of the temperature of either extremity. There was no edema. Several segmental surface veins about the medial malleolus of the left leg were tender and red and indicated inflammatory changes. In the midtibial region of the medial aspect of the right leg there was a segment of vein approximately 5 cm. in length which was red, tense and moderately tender to palpation. The patient was given conservative therapy and responded to the prophylactic therapeutic regimen. This case demonstrates the early process of migratory polyphlebitis.

CASE 3.—The patient, James C., aged 39, was admitted to Kings County Hospital Feb. 1, 1946. He presented a history of having had frostbite twenty years before. Five years later he had trouble with his veins, the nature of which he did not recall. About five years before I saw him he noticed hardened, reddened areas about his legs, which were tender to touch. These areas would disappear for a period of several months and then would occur in the opposite leg. This caused him no distress or discomfort except for the fact that nocturnal edema developed on several occasions. He entered the hospital at this time because of severe pain in both legs. At this time he has a classic picture of thromboangiitis obliterans. This patient demonstrates a past history of migratory polyphlebitis which was characterized by exacerbations and recrudescences over a period of twenty years. Finally he sought medical care because of characteristic changes subsequent to classic thromboangiitis obliterans.

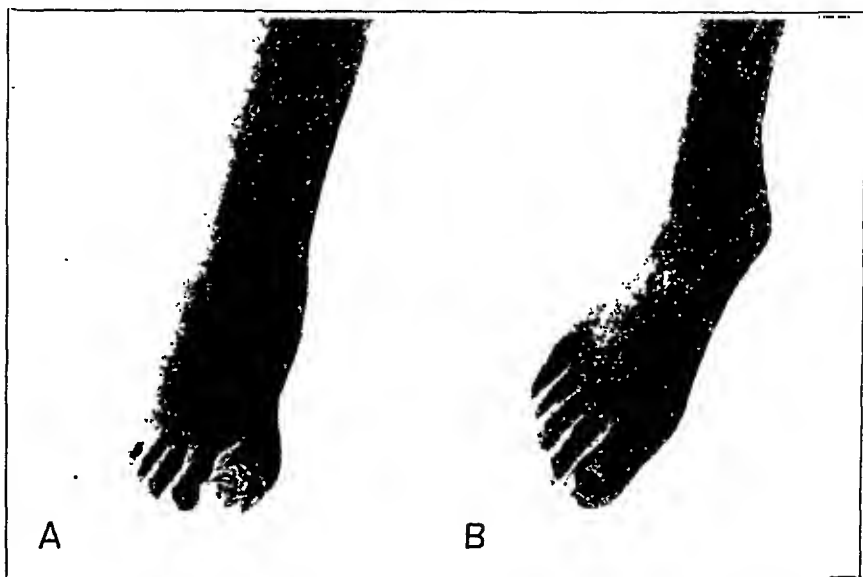


Fig. 1.—A, photograph of the foot of the patient in case 3, illustrating classic thromboangiitis obliterans in a patient with a previous history of migratory polyphlebitis. B, photograph of the foot of the patient described in case 4, illustrating the healing phase of migratory polyphlebitis, with desquamation of the skin over the involved vein. Trophic changes in the toes are clearly demonstrable.

CASE 4.—The patient, John F., aged 26, was brought to the hospital after exposure, which produced what was thought to be frostbite of both toes. He entered the hospital on Feb. 4, 1946, with a history of drunkenness following which he slept out-of-doors in the snow, finally being brought to the hospital. Examination revealed significant findings in both lower extremities. There were segmental involved venous radicles in the feet and in the thighs. These revelations indicated typical migratory polyphlebitis. This patient responded to conservative therapy and has progressed to the chronic stage, with pigment formation and the production of goose-quill-like veins.

These cases demonstrate the multivarious aspects of migratory polyphlebitis. The possible complications and the eventual course of the disease are clearly unfolded.

## DIFFERENTIAL DIAGNOSIS

The characteristic features of migratory polythrombophlebitis are as follows:

1. The disease involves superficial venous segments in the early stages.
2. Discrete nodules form, varying in size from 2 to 4 mm. to 4 or 5 cm.
3. The adjacent veins may contain thrombi.
4. The lesions appear first on the dorsal areas of the feet, legs and forearms and may involve the vessels of the abdominal wall.
5. The acute phase lasts one or two weeks, the lesion disappearing slowly and appearing elsewhere either singly or in groups.
6. When healing occurs, the veins become tense and scarred.
7. Brownish pigmentation with epithelial desquamation occurs over and above the veins when healing commences.

This pathologic process must be differentiated especially from erythema nodosum when the phlebitis is in the anterior parts of the tibial areas. Other forms of nonspecific thrombophlebitis which may occur in varicosities must be eliminated. Phlebitis occurring as a complication of acute febrile disease, erysipelas and similar lesions must be differentiated from migratory polyphlebitis.

## PROGNOSIS AND TREATMENT

As has been previously stated, the appearance of migratory polyphlebitis must be considered as an antecedent to thromboangiitis obliterans. Without adequate treatment, patients with migratory polyphlebitis eventually become candidates for all the complications usually associated with thromboangiitis obliterans. When this occurs the prognosis becomes the same as that of thromboangiitis obliterans. The treatment for this disease entity divides itself into three major groups: (1) prophylactic measures, (2) medical treatment and (3) surgical treatment.

Prophylaxis against phlebitis of this type is of considerable value, especially in postoperative and postpartum patients. Any person presenting a history remotely suggestive of migratory polyphlebitis who must have elective operation not related to his circulatory system should be considered for early ambulation following operation. It has been our policy for all patients after operation to perform motion of the feet as early as possible. The patient is instructed to move the ball of each foot up and down as often as possible. The motion is similar to stepping on the gas of an automobile. One or both feet are moved at the same time. The patient is instructed that these exercises should be done almost a thousand times in twenty-four hours.

Patients who have a past or present history of migratory polyphlebitis are asked to avoid vasoconstricting-affects of cold water. They are also instructed most thoroughly in the general care of the feet. These patients must absolutely eliminate smoking.

Conservative medical treatment is a most satisfactory method in early cases of migratory polythrombophlebitis. In this stage of the disease, venous compression at regular intervals is a most valuable therapeutic measure. This procedure relieves pain and accentuates the disappearance of the acute lesions. The use of Ace bandages is a recommended procedure during an acute attack. The patient may be placed at rest in bed, with elevation of both legs and application of dry heat to the areas involved. The use of chemotherapeutic drugs and/or penicillin has been employed.

Surgical intervention is indicated in cases of deep migratory polyphlebitis when there is much pain, tenderness and edema. In these circumstances, lumbar sympathectomy has been employed most efficaciously. There has been no tendency toward pulmonary embolism in the acute stages of migratory polythrombophlebitis. In the event that sublethal pulmonary embolism should occur, venous ligation would be advised. I have not employed lumbar sympathectomy in any of my cases. When the classic picture of thromboangiitis obliterans develops, the patients are subjected to the same regimen as prescribed for the treatment of those with thromboangiitis obliterans. Any complications arising are treated similarly to those arising in thromboangiitis obliterans.

Miss Dorothea E. Chamberlain aided in the preparation of the manuscript, and Mr. John C. Knight aided with the photography.

## SURGICAL APPROACH TO HYPERTENSION

### Second Report

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AND

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IN A previous report from the University of Illinois College of Medicine, de Takáts, Heyer and Keeton<sup>1</sup> presented the classification, the preoperative study, the selection of cases and the surgical procedures employed, together with the results of follow-up studies of hypertensive patients. Of the methods for splanchnic nerve section, the transdiaphragmatic method of Smithwick<sup>2</sup> gave by far the best results. The selection of patients with early hypertension and the use of this improved technic seemed to us the two important factors in the obtaining of good results. An attempt was also made to analyze the mechanism of relief in hypertensive patients after splanchnic section. Aside from the actual lowering of blood pressure, a slow, gradual improvement of cardiac and renal function, a postural hypotension with consecutive decrease in effective circulating blood volume and a decrease in reflex nervous irritability due to adrenal denervation were mentioned as contributing to the subjective and objective relief obtained.

In this report we wish to present additional experience with the transdiaphragmatic approach to the splanchnic nerves, which has now been performed on a total of 109 patients (table 1). The material is still small and undoubtedly will continue to remain so because of our increasingly rigid criteria for operability.

### SELECTION OF PATIENTS FOR OPERATION

The preoperative study has been detailed in our first communication.<sup>1</sup> This has remained unchanged except that a simple practical work-up

From the Department of Surgery, University of Illinois College of Medicine, St. Luke's Hospital and Research and Educational Hospitals.

1. de Takáts, G.; Heyer, H. E., and Keeton, R. W.: The Surgical Approach to Hypertension, *J. A. M. A.* **118**:501 (Feb. 14) 1942.

2. Smithwick, R. H.: A Technique for Splanchnic Resection in Hypertension, *Surgery* **7**:1, 1940.



now consists of a three day period. On the first day, a basal metabolic rate and an electrocardiogram are obtained and blood is drawn for the determination of blood sugar, nonprotein nitrogen, urea nitrogen and cholesterol; blood counts, the sedimentation rate and a specimen of urine are obtained. An Addis count is done on the urine if the medical consultant thinks that it is indicated. The medical consultant sees the patient before and after the completion of the tests. The eye consultant describes the fundus, grades it and has the opportunity to reexamine it after the operation. Many photographs of fundi have been taken. The history, taken by the intern, checked by the resident and reexamined by the surgeon, is naturally interested in hereditary traits, in childhood diseases with manifest glomerulonephritis or pyelonephritis, in trauma to the lumbar region with manifest hematuria, in exposure to lead and arsenic and in other causes of recognizable renal damage. The neurogenic factor is carefully considered, and occasionally a neuropsychiatric consultation is held. The endocrine factor is evaluated,

TABLE 1.—*Number of Cases of Surgically Treated Hypertension During Ten Year Period*

| Period     | Years     | Number of Cases |
|------------|-----------|-----------------|
| 1          | 1934-1940 | 30 *            |
| 2          | 1940-1943 | 52              |
| 3          | 1944      | 27              |
| Total..... |           | 109 †           |

\* J. A. M. A. 118:501, 1942

† Over 150 patients have follow-up records.

and pituitary, thyroid, adrenal and ovarian involvement is looked for. If obesity is present, a reduction in weight is attempted even if the patient seems operable. The significance of metabolic rates will be discussed later.

The second day is spent on studies of renal function. A concentration-dilution test, a fifteen minute phenolsulfonphthalein test and a urea clearance test are ordered. The Lashmet-Newburgh concentration test is valuable but places too much hardship on the patient, so that urinary concentration is carried out only overnight, from 6 p. m. to 9 a. m. An intravenous pyelogram and a roentgenogram of the chest, at a distance of 2 meters, are taken.

The third day, in which the study is usually completed by noon, is utilized to study the vasomotor reactivity of the patient. This includes the cold pressor test, the test with 9 grains (0.58 Gm.) of sodium amytal and the test for epinephrine and carbon dioxide sensitivity.<sup>2a</sup>

2a. Recently a pressor test by breath holding and a depressor test by combining hyperventilation with pressure on one carotid sinus have been added (Gubner, R.; Silverstone, F., and Ungerleider, H. E.: Range of Blood Pressure in Hypertension, J. A. M. A. 130:325 [Feb. 9] 1946).

On the teaching service at the Research and Educational Hospitals, a number of other tests having teaching or research value are determined. With the help of the medical service of Dr. R. W. Keeton, whose interest in this problem has been unfailing, glomerular filtration rate and total renal blood flow were determined by the inulin-diodrast clearance. Spinal fluid pressures are measured. Eyegrounds have been photographed before and after operation by Dr. R. W. Riser. Vital capacity is determined. All these methods may serve as a basis of a better understanding of the problems, but the short, two and one-half day, work-up is eminently satisfactory for the sizing up of the situation. We doubt that a prolonged study ever leads to any practical conclusion not reached by the short work-up.

The four grades of Wagener and Keith, as tabulated in our first communication, are closely followed. They need not be described again, since any one engaged in this work must be familiar with the classic monograph.<sup>3</sup> It has become increasingly clear, however, that a purely mechanical grading of hypertensive patients is fraught with pitfalls. A patient may have serious myocardial damage due to coronary occlusion and yet have grade 1 retinopathy or grade 1 renal involvement. Again, the renal involvement does not have to run parallel with retinal sclerosis. Aortic or arteriolar sclerosis may be more advanced than the visceral involvement. For this reason we have adopted, purely for our own intercommunications, the following grouping referring to operability.

The first group consists of persons in whom there is a clearcut indication for operation. The ages of these patients do not exceed 40 years. The younger they are the more progressive the disease is apt to be. Their family histories are often burdened with cases of hypertension. Their eyegrounds show no changes or slight narrowing of arterioles; arteriovenous compression may be present. Their systolic pressure varies from 200 to 150 mm. of mercury and the diastolic from 120 to 100; if they are below 20 years, a diastolic pressure of 90 is acceptable. The pressure comes down to normal at rest or during natural or artificial sleep induced with sodium amytal. The heart shows no or minimal changes, the urine is normal and all renal tests show normal function, with the exception of the inulin-diodrast clearance, which is extremely sensitive but is subject to a great deal of error.

This group is obviously the group 1 of Wagener and Keith, but in addition we include in it some of the early, adolescent hypertensive patients who are completely asymptomatic but have a bad family history and show exaggerated vasomotor reactivity. To this group belong

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3. Wagener, H. P. and Keith, N. M.: Diffuse Arteriolar Disease with Hypertension and the Associated Retinal Lesions, *Medicine* 18:317, 1939.

also a number of persons with transient hypertension, so clearly defined by Robert Levy and his associates.<sup>4</sup> Their careful follow-up of young persons who are vascular hyperreactors indicated that they were not good risks for the Army, nor do they do well in civilian life, as individual observations amply demonstrate.

CASE 1.—Fred W., 58 years old, has known of his hypertension since the age of 20. It was then noted that his blood pressure fluctuated a great deal and that it became normal on rest and rose on emotion, physical or mental stress. He smoked and drank rather heavily through his thirties. Early in his thirties attacks of gout began, severest in the spring, activated by alcoholic or dietary excesses. For twenty years he has been on a diet low in purine and has stopped drinking. His blood pressure still fluctuated, but the basal pressure at rest never dropped below 155 systolic and 90 diastolic, whereas it would rise to 180 systolic and 120 diastolic on many occasions.

On entrance to St. Luke's Hospital, July 5, 1943, the right foot was in a state of impending gangrene. It was swollen and cyanotic. The pedal pulses were absent on both sides. The histamine flares did not appear above the right ankle but did appear below the right knee. Paravertebral block with procaine hydrochloride relieved the pain but did not warm up the toes. Evidence of arteriosclerosis was found in the eyegrounds, in the heart and in the kidneys. However, the heart had not enlarged; while forty years after the onset of his hypertension he was still in the stage of benign nephrosclerosis, with hypertension which could still be lowered on rest, nevertheless the widespread vascular sclerosis may well be attributed to the hypertension of long standing.

*Comment.*—Such a history should be compared with the histories in cases of young hypertensive patients in their twenties who have undergone splanchnic nerve section; this would require a thirty to forty year follow-up of the surgical patients, which another generation of surgeons will have to publish. Suffice it to say that the fluctuating juvenile hypertension, even if it does not become malignant in its later stages or even if it does not reach excessive levels, may cause widespread vascular damage. The coronary sclerosis of this patient and the resulting myocardial damage may be responsible for the fact that after forty years his blood pressure is only moderately elevated. He now belongs in group 2.

Included in this first group are some of the patients who have more advanced vascular damage in the retina, the heart and the kidney but who relax under sodium amytal to a diastolic pressure of 100 mm. of mercury. The separation of such patients into one group has been brought about by the fact that when these persons have undergone a technically complete splanchnic section the results have been excellent. Seventeen patients have detailed follow-up records in this series.

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4. Levy, R. L.; White, P. D.; Stroud, W. D.; and Hillman, C. C.: Transient Hypertension: The Relative Prognostic Importance of Various Systolic and Diastolic Levels, J. A. M. A. **128**:1059 (Aug. 11) 1945.

The second group consists of patients in whom operability is debatable. The only argument for operating on these patients is the fact that some of them obtain unexpected objective and subjective relief whereas others have a slightly lower pressure, but the organic damage is naturally permanent and progressive. The advanced cases of group 2 and the early cases of group 3 of Wagener and Keith fall into this category. The ages of the patients may vary from 20 to 55; they have pronounced retinal sclerosis, recurrent angiospasm and even an occasional retinal hemorrhage. The diastolic pressure cannot be lowered below 110 mm. of mercury by any method. The heart is enlarged; there may be angina pectoris. The urine contains casts and albumin but no red cells. The Addis count is helpful in this group; a certain permissible number of red cells is always present by this method. The renal function is impaired, but urea clearance should not be below 50 per cent of normal. Cerebral accidents may already have occurred, with only temporary functional loss.

Obviously the patients in this group suffer from greater or smaller amounts of organic vascular damage. Twenty-eight patients have been operated on in this series; remarkable results have been obtained in a group of toxemic or eclamptic women in whom severe vascular damage occurred but in whom the damage did not continue to operate so that progress was arrested. Patients with healed glomerulonephritis or pyelonephritis with negative urinary findings and normal sedimentation rates may be included. In fact, only the renal biopsy reveals the origin of the hypertension. This special group of patients with renal hypertension will be discussed in more detail.

The third group consists of patients in whom splanchnic section is not indicated. To this group belong the late group 3 and all the group 4 patients of Wagener and Keith. Such patients have large recurrent hemorrhages or exudates in the retina; many of them have papilledema. The diastolic pressure is extremely high and may range from 170 to 120. It is fixed. Congestive or anginal cardiac failure is often present. The urine contains albumin, casts and red cells. The urea clearance is less than 50 per cent of normal and the concentrating ability of the kidney is below 1.015. Cerebral accidents have been numerous. The patient is in an actual or impending state of malignant hypertension. Five such patients have been operated on, and a large number of others have not been accepted for operation. No effect on the course of the disease was noted in this group.

To this group belongs also an important group of patients in whom some definite causative factor was responsible for the hypertension but could be readily overlooked. We have in mind 2 juvenile patients with hypertension referred to us for operation, who had coarctation of the

aorta. In 1 the femoral pulses were hardly palpable and erosion of the ribs was pronounced; in the other patient the diagnosis was less simple, since femoral pulses were good and the configuration of the aorta on roentgenologic examination was not typical. However, the difference in the oscillometric curves of the upper and lower extremities and the partial arterial block of the left subclavian artery led us to search for erosion of the ribs. Also a slight murmur in the left scapular region helped.

The presence of chronic or recurrent pyelonephritis equally contraindicates an operation. This is not to say that a completely "burned-out" lesion resulting in scarring and arteriolar sclerosis would not yield to operation, because we have such patients in our second group. It takes, however, an experienced and mature internist to detect these conditions, and often a diagnosis of essential hypertension is made since neither the history nor the urinary findings are suggestive. Smithwick<sup>5</sup> has just reported on a group of 11 pyelonephritic patients on whom splanchnic nerve section has been performed, with notable results. Attention should also be called to a large group of patients with slowly progressive hypertension suffering from arteriosclerosis of the aorta and its larger branches; they exhibit a high pulse pressure. They are not particularly suitable for operation, since the lowering of pressure will produce symptoms of decreased coronary or renal blood flow.

When the hypertension fluctuates greatly and is accompanied with rises in blood sugar, a chromaffin tumor of the adrenals can be suspected. The point should be stressed, however, that the fluctuating phase may later be followed by persistent hypertension, producing diffuse vascular damage.

Hypertension is often present in cases of tumors of the adrenal cortex and is especially suspected in cases of hirsutism, obesity and erythrocytosis. The attempts to differentiate these conditions from pituitary basophilism are not always successful. Whereas the ovaries can be palpated or inspected during exploration, the roentgenogram of the sella turcica and a sugar tolerance test are often unrevealing.

Both medullary and cortical adenomas may be encountered during the routine exploration of the kidney and adrenals, which is done at the time of the splanchnic section. The decision at this time to remove or resect a suspiciously large adrenal is not easy and if the operation is done it should be immediately followed by 20 cc. of adrenal cortex extract given intravenously. It should also be noted that both pituitary and

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5. Smithwick, R. H.: Surgical Treatment of Hypertension: The Effect of Radical (Lumbodorsal) Splanchnicectomy on the Hypertensive State of 156 Patients Followed One to Five Years, *Arch. Surg.* **49**:180 (Sept.) 1944.

cortical adenomas producing neither sexual changes nor hypertension can be found at autopsy.

#### PREMEDICATION AND ANESTHESIA

In the present series all operations were done with identical technic. Premedication consisted of a light dose of barbiturate, such as 1.5 grains (0.09 Gm.) of pentobarbital sodium, for the night preceding the operation. One hour preceding the induction of anesthesia morphine-scopolamine was given in a 25 to 1 ratio, mostly  $1/6$  grain (0.01 Gm.) of morphine to  $1/150$  grain (0.0004 Gm.) of scopolamine. For women of slight build, weighing less than 125 pounds (56.7 Kg.),  $1/8$  grain (0.007 Gm.) of morphine to  $1/200$  grain (0.0003 Gm.) of scopolamine is preferable. The anesthetic preferred is ether administered intra-tracheally with the open drop method, with nitrous oxide and ether induction. In our earlier cases cyclopropane was used frequently, but too often cardiac irregularities were encountered on dissecting or pulling of the splanchnic nerves. In fact, because of reflexes originating from the stimulation of these nerves, the area can be advantageously flooded with 1 per cent procaine hydrochloride.

Because of the vicinity of the pleura and the necessity of separating pleural adhesions from the diaphragm or the posterior mediastinum, breathing must be even, not labored and not too deep. Also the accumulation of carbon dioxide must be prevented as much as possible. Such patients are definitely sensitive to the accumulation of carbon dioxide and respond with a rise in blood pressure and a pronounced venocapillary oozing. The oozing may be due to the peripheral action of carbon dioxide on blood vessels under deep anesthesia. Just as patients with toxic diffuse goiters require a great deal of oxygen and are exceedingly sensitive to the lack of it, hypertensive patients seem to tolerate the closed method with the absorption technic not so well as when drop ether is used with the tracheal tube in place or when a semiclosed ether-oxygen mixture is given without rebreathing and a flow of 10 liters of oxygen per minute is maintained. A one way valve is useful to blow off the expired carbon dioxide. With the cooperation of Dr. F. C. Jacobson, director of anesthesia at St. Luke's Hospital, we studied the reaction of some hypertensive patients to 10 per cent carbon dioxide administered for three minutes. The hyperventilation and rise in blood pressure were variable, but the sensitivity of some patients was pronounced and convulsive seizures or extreme restlessness necessitated the termination of the experiment (figs. 1, 2 and 3).

The problem of anoxia, hypercapnia and acapnia during such operations merits further study. Suffice it here to say that, as Gellhorn has shown for the experimental animal, the rise in carbon dioxide may

cause a pronounced rise in blood pressure in the lightly anesthetized or nonanesthetized patient, but the same concentration may cause a deep fall together with peripheral vasodilatation in the patient under deep narcosis.<sup>6</sup> That a pneumothorax accidentally produced may further complicate the situation by hypoventilation and inability to blow off the excess carbon dioxide seems obvious.

We have been impressed with the necessity of expert anesthesia and the closest interchange of ideas between a well trained anesthetist and the surgeon. In addition to maintenance of a free airway and control of the depth of anesthesia, the proper attention to signs of carbon dioxide accumulation are important. We have had our best exposures and favorable anatomic conditions greatly complicated by diffuse oozing, by hyperventilation and occasionally even by convulsions, which necessitated

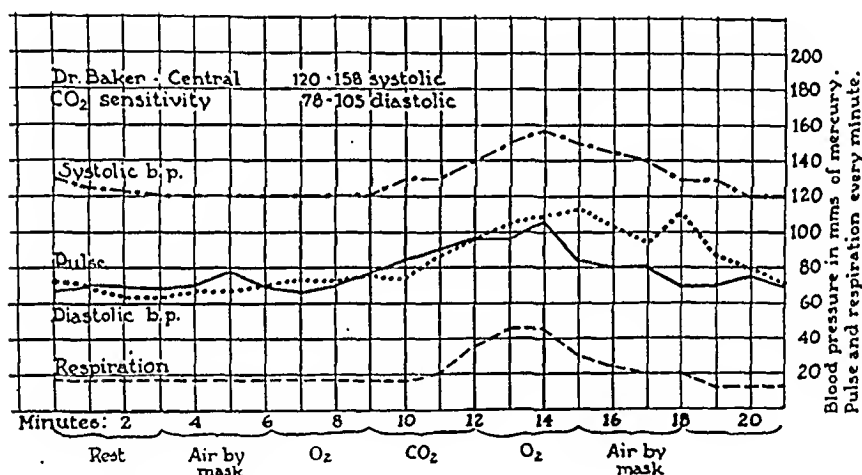


Fig. 1.—Pressor response to 7 per cent carbon dioxide in a young, normotensive man. After control periods with rest, air and oxygen by mask, none of which affected the patient's blood pressure, pulse rate or respiratory rate, carbon dioxide was administered for three minutes. Two minutes after the first whiff, all lines are seen to rise, the peak being reached two minutes after the carbon dioxide has been discontinued. This is a typical, normal response.

the postponement of some part of the operation to a later stage. Thus, in this series of 52 patients, the customary two stage operation had to be broken up into three stages in 3 patients because of conditions brought about by anesthesia.

Recently two timely articles have appeared on the importance of anesthesia during splanchnic nerve section. Haugen<sup>7</sup> recommended

6. Gellhorn, E. A.: *Autonomic Regulations: Their Significance for Physiology, Psychology and Neuropsychiatry*, New York, Interscience Publishers, Inc., 1943, pp. 23-27.

7. Haugen, F. M.: *Hypertension: Management of the Anesthesia Period*, *Anesth. & Analg.* 22:152, 1943.

induction with 2.5 per cent pentothal sodium to facilitate induction and avoid the anoxemia during the stage of excitement; he also advocated the same drug when blood pressure rises because of carbon dioxide excess and after respiratory obstruction is relieved.

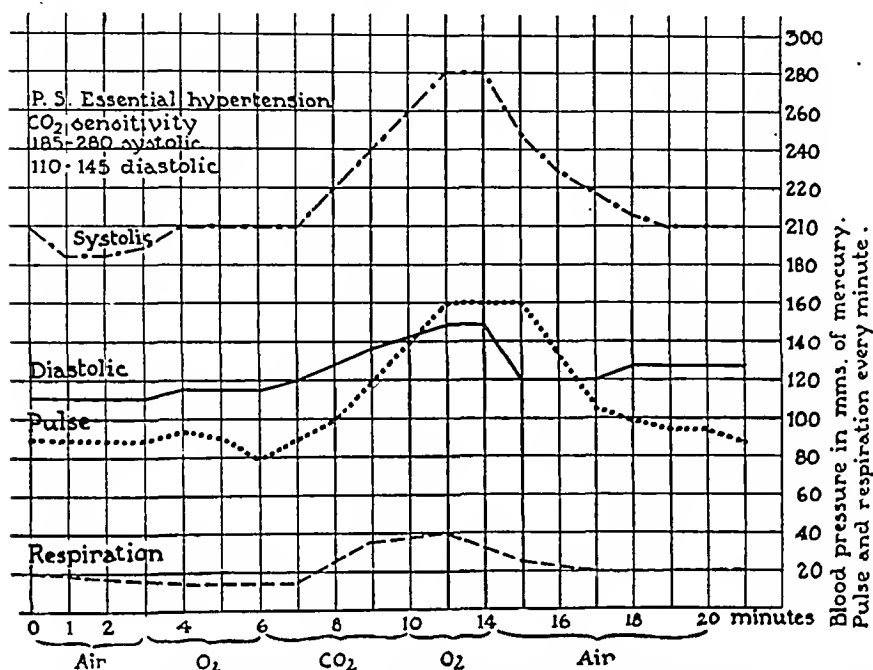


Fig. 2.—Pressor response to carbon dioxide. The same technic was used as in figure 1. Note the rise from 185 to 280 systolic and 110 to 145 diastolic pressures. The pulse rate rose from 110 to 160 a minute. This patient showed great sensitivity to carbon dioxide.

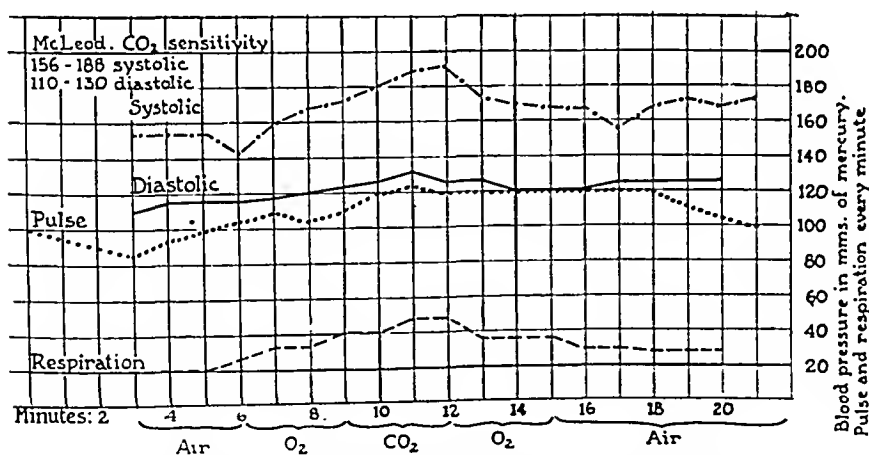


Fig. 3.—The response of this patient showed little change from normal. His blood pressure showed little response to sympathectomy. The renal biopsy showed advanced nephrosclerosis with irreversible renal damage. While he was nervous and jittery and his condition was classified as "neurogenic" hypertension in another institution, his lesion at the time of operation was predominantly renal with severe vasoconstriction.



Phelps and Burdick<sup>8</sup> favored cyclopropane but mentioned that it may produce bronchospasm, which in turn is readily abolished by atropine, 1/150 grain (0.0004 Gm.) to 1/75 grain (0.0008 Gm.), given intravenously. We have had such an experience; changing to ether readily abolished the spasm. The authors also warned of rises of blood pressure during induction, during a stormy or prolonged second stage or from a disturbance of oxygen-carbon dioxide balance. Their article properly states that too little attention has been given to anesthetic procedures during surgical operations for hypertension.

This point requires emphasis because during conditions of war it has been necessary to operate with fewer expert anesthetists. If the surgeon has a good grasp of some of the principles involved, he may tide his patient over a critical situation. The anesthetist is such an important part of the surgical team that his absence or incompetence severely handicaps the operation. The fall in blood pressure occurring during various positions and immediately after section of the splanchnic nerves will be dealt with in the next paragraph.

#### THE COURSE OF THE OPERATION

After the patient has been intubated and his respiration and blood pressure stabilized, he is slowly turned over to a prone position. As is well known to anesthetists, this change of posture alone may bring about a further fall in pressure. In order to permit proper ventilation, a well inflated horseshoe cushion is placed on the table before the patient is rolled over from the cart. The break of the table, shown in figure 4A, has been lately abandoned, since it often contributes to a further fall in pressure and does not really facilitate exposure; it may help in resection of the twelfth rib. Instead of this position we now tilt the patient about 30 degrees to the side, with the surgical field raised toward the operator. This permits the flexion of the knee and hip of the side to be operated on, which relaxes the psoas muscle and greatly aids in removing the lumbar sympathetic chain from this angle.

The skin has been prepared with iodine and alcohol. Prior to the preparation the line of incision is marked on the skin with a 2 per cent aqueous solution of brilliant green (tetraethyldiaminotriphenylmethane sulfate). The incision starts at the level of the ninth rib at the well palpable outer border of the sacrospinalis muscle. After it reaches the level of the twelfth rib, it swings laterally along its course and gently curves toward the anterior-superior spine of the iliac bone, without quite reaching it. The skin marking is important since it obviates the palpation of the prepared skin for landmarks, which should be avoided. If the

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8. Phelps, M. L., and Burdick, D. L.: Anesthetic Management of Patients Undergoing Sympathectomy for Hypertension, *Anesthesiology* 4:361, 1943.

twelfth rib is not readily palpable because it is too short or the patient is too obese, it is well to have one of the pyelograms of the patient on hand, which readily denotes the length and course of the rib.

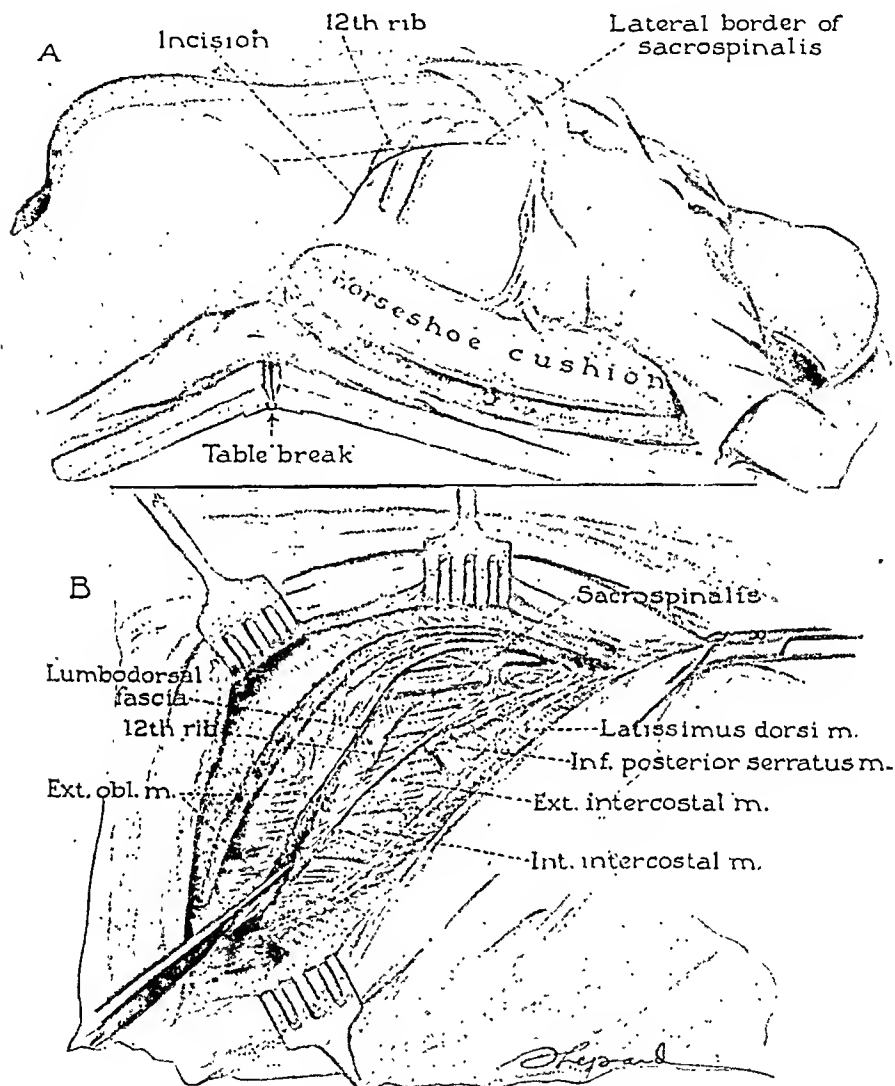


Fig. 4.—A, position of the patient on the operating table. An inflatable rubber cushion is placed below the chest, permitting expansion of the thoracic wall. The table is broken to develop the space between the twelfth rib and the iliac crest. The kidney rest is not elevated, as its pressure on the upper part of the abdomen often produces depressor reflexes and may also compress the vena cava, thus decreasing venous return to the heart. The incision starts at the palpable lateral border of the sacrospinalis muscle, follows the twelfth rib and curves gently toward the anterior-superior portion of the spine. B, the muscles of the back are cut along the line of the incision in the skin. The latissimus dorsi and the inferior posterior serratus muscles are well defined. Below them the lumbodorsal fascia is visualized. The incision is carried down to the twelfth rib. At the lower angle of the incision the oblique abdominal muscles become visible. Failure to identify and dissect these layers greatly handicaps adequate closure of the wound in layers.

To expose the twelfth rib the incision is carefully made through anatomic layers, since the reconstruction of the wound is thus facilitated (fig. 4*B*). The latissimus dorsi, the inferior posterior serratus muscle

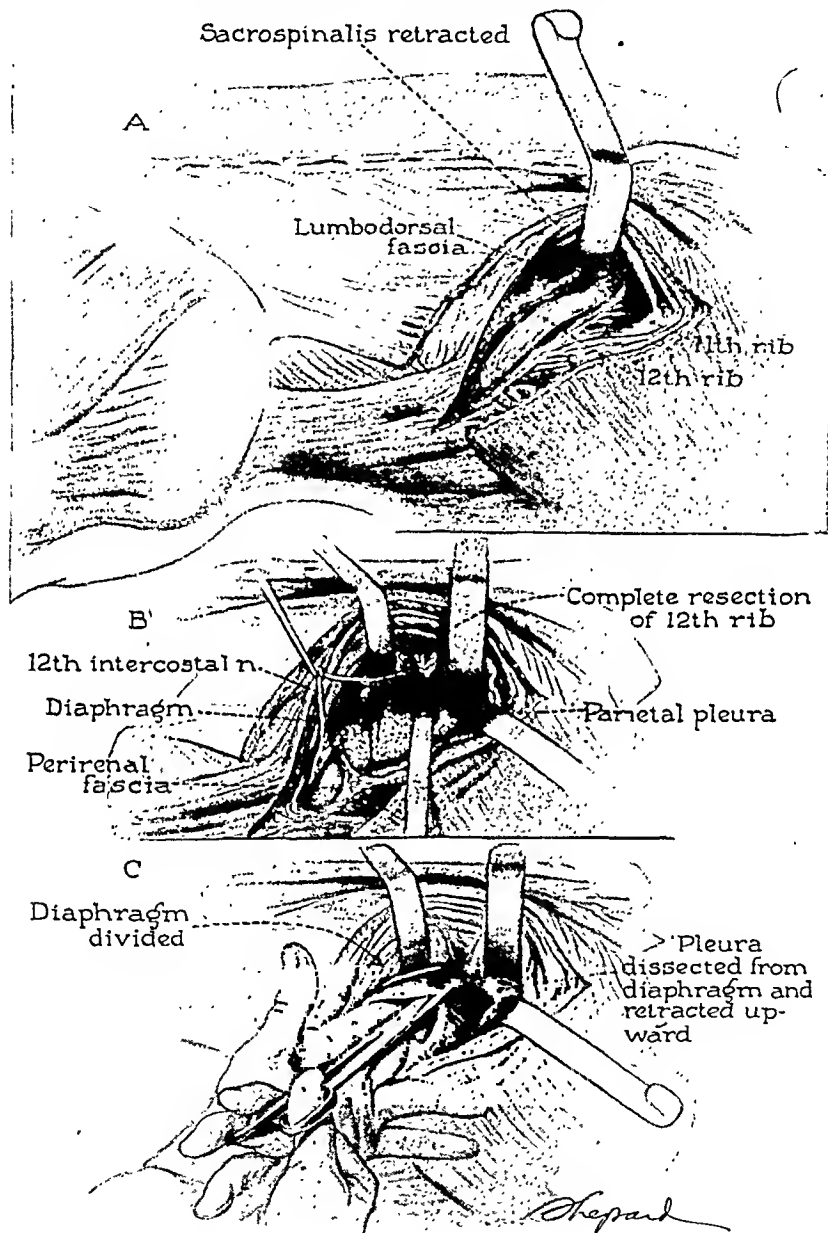


Fig. 5.—*A*, the edge of the sacrospinalis muscle is retracted so that the proximal end of the rib can be visualized. The twelfth rib is then resected from its tip to its articulation with the vertebra, which leaves a smooth articular surface. *B*, the resection of the rib is completed. At the lower angle of the wound the perirenal fat shines through the fascia. More medially the fibers of the diaphragm become visible. The pleura is often adherent to the diaphragm, and its edge should be carefully defined. *C*, the pleura has been bluntly pushed cephalad. The diaphragm is sectioned toward its vertebral attachment.

and the lumbodorsal fascia are divided. There is usually little bleeding unless the patient's venous pressure is high from straining or unless he is accumulating carbon dioxide under deep anesthesia. The edge of the sacrospinalis muscle is defined and mobilized, since retraction of this muscle toward the midline is important (fig. 5A). The twelfth rib is now removed in toto subperiosteally, by which we mean that the rib is exarticulated at the costovertebral joint. This leaves a smooth surface and allows better exposure of the thoracic sympathetic chain than if the rib is simply resected. After the removal of the rib, the pleura, the diaphragm and the perirenal fascia come into view. The twelfth intercostal nerve is resected from the lateral edge of the wound as close to the intervertebral foramen as possible (fig. 5B). The diaphragmatic pleura may be well defined as it spreads over the leaf of diaphragm, but it may also be obscured by adhesions, since a diaphragmatic pleurisy seems to be a remarkably frequent occurrence. The diaphragmatic pleura must be sharply or bluntly dissected from the diaphragm, since the diaphragm will have to be cut toward the spinal column, where the sympathetic chain and splanchnic nerves traverse it (fig. 5C). There are few bleeders in the diaphragm, which can be readily clipped with new silver clips. Cotton sutures may be placed as guy sutures and tied at the completion of the operation. The pleura now is peeled off the spinal column as high as the fingers of the operator will reach, thus exposing the posterior mediastinum. The anatomic structures which this operation must visualize are shown in figure 6A. When the parietal pleura is peeled off, the thoracic chain and splanchnic nerves become visible to the midthoracic level. The major splanchnic nerve can be seen to enter the celiac ganglion, which should also be visible. If the perirenal fascia and the peritoneum are peeled off, the lumbar sympathetic chain is exposed just medial to the psoas muscle. When the hip and knee are flexed and the patient is turned in a semilateral position, this exposure is greatly facilitated. The entire field is best exposed by four Deaver retractors, and a head lamp is used for illumination. The structures removed are shown in figure 6B. The major splanchnic nerve is clipped at the fifth or sixth thoracic level, a segment which cannot always be reached, because of adhesions or because of the shape of the thorax. As long a segment is excised as anatomically possible. Distally the nerve is transected at its entrance into the celiac ganglion. Often the minor and minimal splanchnic nerves are seen and cut, but no special effort is made to look for them, since the thoracic ganglions from which they originate are removed. The sympathetic ganglionated trunk is excised from the ninth dorsal to below the second lumbar ganglion. Clips are placed on the divided ends of the nerves to impede regeneration and also to enable a check on the level of transection by a roentgenogram.

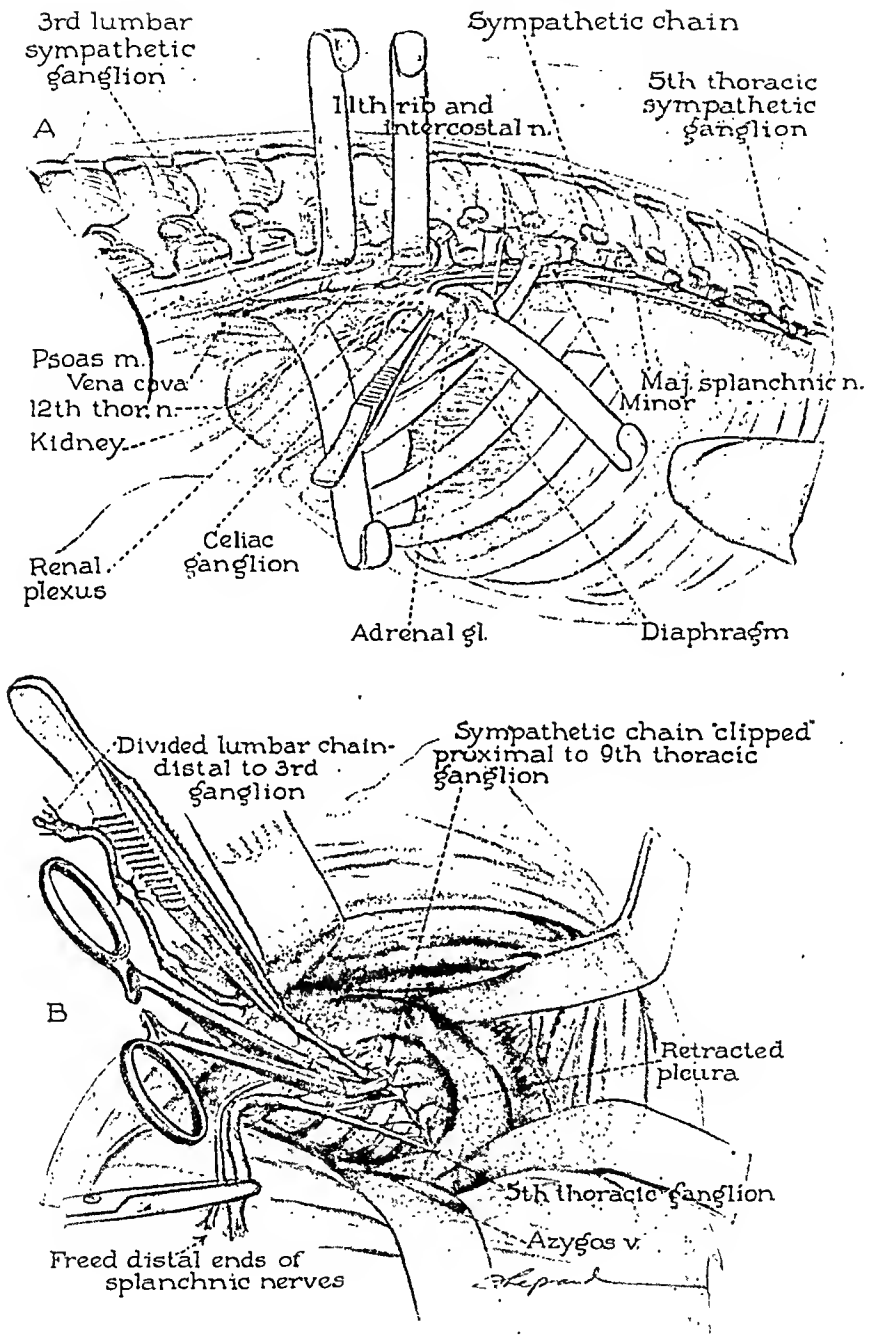


Fig. 6.—*A*, the anatomy of the splanchnic nerves and sympathetic chain as it is exposed in stages during the operation. The twelfth rib has been removed. The sympathetic chain and intervening ganglia are shown in black, and the splanchnic nerves are shown in white. The pleura, vena cava (on the right) and the psoas muscle are retracted. *B*, the actual operative procedure. The sympathetic chain is removed between the ninth dorsal and the third lumbar ganglion; the major splanchnic nerve from the fifth dorsal ganglion to its entrance into the celiac plexus. The diaphragm and kidney are not shown.

To facilitate exposure a part of the eleventh rib is resected when the twelfth is rudimentary.

Next the perirenal fascia is entered. The kidney is adequately exposed and its size, appearance and consistency noted. The renal pelvis and ureter, the renal vessels and the adrenal gland are palpated and if necessary exposed. Finally a long narrow pedicle is cut from the sacrospinalis muscle, an oval-shaped biopsy specimen is taken from the convexity of the kidney or wherever scarring or pitting is visible and three no. 20 cotton sutures are taken to secure the muscle flap into

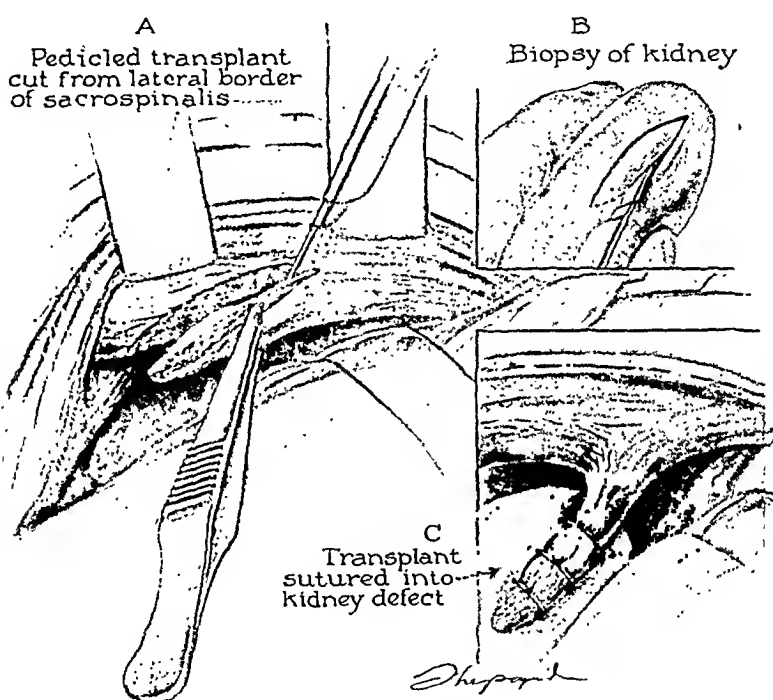


Fig. 7.—The kidney, ureter, renal artery and adrenal gland are palpated. An elliptic incision is made into the cortex of the kidney, and a previously prepared muscle flap is swung into the defect and anchored with three no. 20 cotton sutures. The muscle graft serves the triple purpose of hemostasis, nephropexy and possible revascularization through extrarenal channels.

the renal defect. This muscle graft not only stops bleeding but may serve as an avenue of collateral circulation<sup>9</sup> (fig. 7).

Naturally, if there is suggestive evidence in the preoperative studies of definite renal or adrenal involvement, the exploration of the kidney precedes the splanchnic section and the dorsolumbar sympathectomy.

The reconstruction of the wound is simple. No sutures are placed in the cut segment of the diaphragm, since frequent fluoroscopic studies

9. de Takats, G., and Scupham, G. W.: Revascularization of the Ischemic Kidney, *Arch. Surg.* 41:1394 (Dec.) 1940.

have revealed no detectable impairment of respiratory function. In the earlier operations the muscle was sutured, which seems to account for more splinting and pain in respiration and possibly some pleural reaction. In suitable cases one may avoid cutting the diaphragm at all, by exposing the dorsal and lumbar chains above and below the diaphragm. This exposure, however, may necessitate the resection of the eleventh rib in addition. The cut muscles are sewed in three layers, and interrupted skin sutures are placed in the skin.

Throughout the operation isotonic solution of sodium chloride is administered intravenously. Unless an alarming fall in blood pressure occurs or a severe hemorrhage is encountered, no other fluid is given for the first stage, which is usually done on the right side. For the second stage, which is done from ten to twenty days after the first, from 500 to 1,000 cc. of blood are given routinely during the operation. While the drop in blood pressure after one splanchnic nerve has been cut is transitory, when the second nerve is cut a severe fall might occur, which is prevented or minimized by the transfusion of blood. Hemorrhage may be cumbersome from an intercostal vessel high up in the thoracic cavity when the dorsal chain is excised. Cushing clips carried on a 10 inch (25.4 cm.) long carrier readily arrest this bleeding. Occasionally hemorrhage may occur from an artery to the diaphragm which retracts, and such hemorrhage is difficult to control. If a tear in the pleura occurs, the operation may proceed without much difficulty except that careful reexpansion of the lung must be done when the wound is closed. Suction may be applied during closure. Small tears can be closed by Cushing clips or fine cotton sutures.

#### THE POSTOPERATIVE COURSE

Before the patient is returned to his room, signs of atelectasis are watched for. Whiffs of carbon dioxide are given to the patient every hour for twelve hours. He may move about freely. Usually 3,000 cc. of fluids are given intravenously the first day and 1,000 cc. the second day, on which the patient begins to take liquids. Morphine is given every six to eight hours to encourage ventilation and alleviate pain.

There has been no postoperative death in this series. Tension pneumothorax had to be aspirated in 3 cases, freeing the patient of respiratory distress. Subcutaneous emphysema developed and readily absorbed in a few cases. Pulmonary atelectasis was seen in 5 patients, bronchopneumonia developing in only 1. In 1 patient a late stitch abscess developed, which drained for six weeks. This patient had chronic acne of the back, which was treated with alcohol rubs and roentgen rays preoperatively, but it was obviously an error in judgment to proceed with the operation. The second side was done four months later,

without any difficulty. There were no other infections. No empyema developed in any of the patients with pneumothorax; fluid was allowed to absorb unless it caused respiratory distress.

Before the patient is discharged from the hospital, the presence or absence of postural hypotension is looked for. Also the signs of sympathetic denervation of both lower extremities are established. Unless this was pronounced, the operation was considered technically incomplete.<sup>2</sup> In older patients one lumbar chain is purposely left uncut. In some patients the preoperative studies are repeated, but this seemed an unnecessary imposition at this early date, so that studies were made only at three month intervals.

#### FOLLOW-UP SYSTEM

On discharge each patient receives copies of a questionnaire, which he is to mail in every three months the first year, every six months the second year and every year after that. The patients coming from the city of Chicago report in person; the out of town patients, who are mostly from downstate, are asked to have their referring physicians fill out the cards; most of them, however, return for one or two visits. The patients were reexamined in the vascular clinic of the University of Illinois College of Medicine or at St. Luke's Hospital.

The questionnaire was made as simple as possible, and many additional data were obtained on certain persons; this represents the

TABLE 2.—*Follow-Up Questionnaire for Patients Operated on for Hypertension*

|   |               |                |        |
|---|---------------|----------------|--------|
| Name.....   | Date.....     |                |        |
| Address.....  |               |                |        |
| 1. Have the following symptoms been   | Relieved      | Improved       | Worse? |
| Fatigue.....  | .....         | .....          | .....  |
| Nervousness.....  | .....         | .....          | .....  |
| Dizziness.....  | .....         | .....          | .....  |
| Palpitation.....  | .....         | .....          | .....  |
| Breathlessness.....   | .....         | .....          | .....  |
| Urinary frequency.....  | .....         | .....          | .....  |
| 2. What is your blood pressure after five minutes in the following positions:   |               |                |        |
| Horizontal:.....  | Sitting:..... | Standing:..... |        |
| 3. What is the specific gravity of the urine in the morning? (Do not drink any fluid after 6 p. m. the night before.) |               |                |        |
| 4. Are you working? Yes..... No.....  |               |                |        |
| Full time.....  |               | Part time..... |        |
| If not working, is this due to your state of health?  |               |                |        |

minimal data obtained (table 2). Of the 52 patients living, records have been obtained of 50, which is the basis of the tabulated results.



TABLE 3.—Results of Surgical Treatment of Hypertension (Grade 1)

| Case | Patient | Age, Yr. | Blood Pressure | Eye-grounds | Blood Pressure Under Sodium Amytal | Blood Pressure Under Vasoeon-striector | Blood Pressure in Horizontal Position | Postural Hypo-tension* | Symptoms                 | Working Ability†                     | Period of Follow-up, Mo. on Basis of 3 |
|------|---------|----------|----------------|-------------|------------------------------------|--|---------------------------------------|------------------------|--------------------------|--------------------------------------|--|
| 1    | E. L.   | 23       | 181/121        | 1           | 120/80                             | .....                                  | 130/80                                | 00/?                   | None                     | 10 hr. day                           | 48                                     |
| 2    | J. W.   | 24       | 150/90         | 1           | 118/80                             | 184/90                                 | 140/80                                | 7/2                    | None                     | 8 hr. day                            | 25                                     |
| 3    | S. R.   | 21       | 141/91         | 1           | 112/71                             | 164/100                                | 140/90                                | 138/104                | Palpitation; nervousness | 8 hr. day                            | 30                                     |
| 4    | L. W.   | 28       | 146/74         | 0           | 110/56                             | .....                                  | 124/64                                | 82/55                  | None                     | .....                                | 18                                     |
| 5    | J. G.   | 15       | 175/125        | 0           | 125/80                             | 160/100                                | 118/80                                | 50/38                  | None                     | In Army                              | 44                                     |
| 6    | R. K.   | 24       | 150/90         | 0           | 120/65                             | .....                                  | 139/92                                | 93/55                  | None                     | 8 hr. day                            | 46                                     |
| 7    | G. L.   | 43       | 150/94         | 1           | 112/82                             | .....                                  | 140/100                               | 123/92                 | None                     | 8 hr. day                            | 16 Incomplete lumbar sympathectomy     |
| 8    | D. W.   | 20       | 160/66         | 1           | 116/70                             | 226/100                                | 120/80                                | 120/75                 | None                     | 8 hr. day                            | 25                                     |
| 9    | R. R.   | 20       | 160/80         | 0           | 118/70                             | .....                                  | 154/80                                | 78/?                   | Few                      | 11 hr. day                           | 37                                     |
| 10   | M. C.   | 35       | 178/120        | 1           | 132/68                             | 190/110                                | 120/105                               | 96/76                  | None                     | Sudden blindness; cerebral accident? | 48                                     |
| 11   | M. S.   | 24       | 146/112        | 0           | 120/84                             | .....                                  | 120/80                                | 0                      | None                     | .....                                | 56                                     |
| 12   | J. W.   | 16       | 158/115        | 1           | 126/94                             | .....                                  | 150/100                               | .....                  | None                     | .....                                | 51                                     |
| 13   | M. Z.   | 21       | 152/99         | 0           | 135/80                             | 190/120                                | 140/80                                | 80/?                   | .....                    | Dead                                 | 47 Sudden death; no cause              |
| 14   | M. S.   | 25       | 152/95         | 1           | 120/76                             | .....                                  | 150/85                                | 72/50                  | None                     | .....                                | 36                                     |
| 15   | D. T.   | 42       | 194/95         | 1           | 108/70                             | 190/100                                | 174/104                               | 69/55                  | Slight headache          | 0 hr.                                | 32                                     |
| 16   | A. S.   | 33       | 153/100        | 1           | 122/70                             | 168/122                                | 120/85                                | 84/56                  | Headache                 | Good                                 | 28                                     |
| 17   | H. F.   | 23       | 135/90         | 0           | 100/80                             | 140/65                                 | 128/100                               | 60/0                   | Fatigue                  | .....                                | 24                                     |

\* Postural hypotension determined before discharge from hospital.

† Postoperative data are the ones obtained at time of last examination.

## RESULTS OF THE OPERATION

The results of transdiaphragmatic splanchnic section have been studied separately in the three groups as defined previously.

*Group 1* (table 3).—Seventeen patients have satisfactory follow-up records in this series, with postoperative periods ranging from eighteen to fifty-seven months. Their ages varied from 15 to 43, but with a few exceptions they were young, the average age being 27.3 years. Their preoperative blood pressures varied from 178 to 146 systolic and 120 to 74 diastolic. After an average follow-up period of thirty-five months, the blood pressures determined with the patients in the horizontal position were from 154 to 120 systolic; the diastolic pressure never exceeded 80 mm. of mercury. Each of these pressures represents the average of many individual determinations. Table 3 represents some of the data on this group of patients; the summary is given in table 4.

TABLE 4.—*Summary of Results of Surgical Treatment of Hypertension (Grade 1) in Seventeen Cases*

|              | Age, Years | Preoperative<br>Blood Pressure,<br>Mm. of Hg | Postoperative<br>Blood Pressure,<br>Mm. of Hg | Period of<br>Follow-Up,<br>Months |
|--------------|------------|--|---|-----------------------------------|
| Maximum..... | 43         | 178/120                                      | 154/80  | 57                                |
| Minimum..... | 15         | 146/74                                       | 120/80  | 18                                |
| Average..... | 27.3       | 157/97                                       | 144/80  | 35                                |

From a study of these charts it would seem as if early, group 1, hypertension could really be checked and brought back to a normal level. While a preoperative diastolic pressure of 74 mm. is shown as the minimum, no patient was operated on who at one time or another did not show a diastolic pressure of 100 mm. of mercury.

In this group belong a number of patients with toxemic, rheumatic and pyelonephritic renal lesions which seem to show a favorable post-operative course, since the original injury to the vascular system of the kidney had subsided and the residual damage was not progressive; these groups will be discussed in more detail under a separate heading.

A few of the 17 case histories in brief abstract may serve better to illustrate the type of response to transdiaphragmatic splanchnic nerve section.

*CASE 2* (table 3, case. 1).—Edward L., a 23 year old laborer, was admitted to the Research and Education Hospitals on Oct. 3, 1940 to determine the cause of his hypertension, discovered during routine physical examination by his company physician. The patient was free of complaints on entrance.

*Past History.*—The patient had been well in every respect and able to carry on heavy manual labor. He had had scarlet fever in 1931. There was no history of renal complication.

*On Entrance.*—The patient's blood pressure was 192 systolic and 100 diastolic in millimeters of mercury. Pentothal sodium given intravenously reduced his blood pressure to 138 systolic and 90 diastolic in millimeters of mercury. Under 9 grains (0.58 Gm.) of sodium amytal the blood pressure fell to 120 systolic and 80 diastolic in millimeters of mercury. On bed rest his blood pressure varied between 190 and 120 mm. of mercury systolic and between 134 and 110 mm. of mercury diastolic. The physical examination was noncontributory. The eyegrounds showed evidence of slight spasm and early sclerosis of the retinal vessels. The urine was normal. Reactions to tests for renal function were within normal limits. An intravenous pyelogram was normal. The electrocardiogram showed no deformities. An insulin tolerance test showed a maximal depression to 86 mg. of glucose in 100 cc. of blood.

*Operations.*—Operations were done October 22 and October 29, the right and left splanchnic nerves and dorsolumbar sympathetic chains being excised.

*Course.*—On discharge the blood pressure in the horizontal position was 130 systolic and 80 diastolic in millimeters of mercury. On standing, the blood pressure was 60 systolic and 0 diastolic in millimeters of mercury. The insulin tolerance test showed a dip to 38 mg. per hundred cubic centimeters of blood. After two months of rest he resumed his previous work. The last follow-up, four years after operation, revealed that he was completely asymptomatic and worked ten hours daily in a defense plant. His blood pressure was 130 systolic and 80 diastolic in millimeters of mercury; the pressure dropped to 100 systolic and 60 diastolic on standing.

*Comment.*—This was a case of asymptomatic early hypertension. There was a history of scarlet fever. The patient has normal blood pressure, with full working capacity, four years after operation.

CASE 3 (table 3 case 8).—Delano W., a 20-year old youth, entered the Research and Educational Hospitals of the University of Illinois College of Medicine on Jan. 21, 1942, complaining of shortness of breath, dizziness, fatigue and nervousness for the past eighteen months.

*History.*—The past history was noncontributory except for scarlet fever while the patient was in high school. The family history was noncontributory.

*On Entrance.*—The patient's blood pressure was 160 systolic and 86 diastolic in millimeters of mercury. The eyegrounds showed grade 1 retinopathy. The electrocardiogram showed a right ventricular preponderance; the roentgenogram of the chest, taken at a distance of 2 meters, showed the heart to be of normal size. The basal metabolic rate was  $\pm 8$  per cent. Determinations of blood chemistry gave normal results. The urinary analysis was noncontributory. The phenol-sulfonphthalein dye excretion in fifteen minutes was 30 per cent, the urea clearance (standard) was 88 cc. per minute. He concentrated urine to 1.037 specific gravity. The intravenous pyelogram was normal. Sodium amytal depressed the blood pressure from 160 systolic and 86 diastolic to 116 systolic and 70 diastolic. The epinephrine sensitivity test revealed a rise from 152 systolic and 80 diastolic to 236 systolic and 100 diastolic.

*Operations.*—Operations were performed on July 7 and July 21, 1942. Both splanchnic nerves were removed from midthoracic level to their entrance into the celiac ganglion. The sympathetic chain was removed from the twelfth dorsal to the second lumbar ganglion on the right and from the ninth to the twelfth dorsal ganglion on the left. On discharge the patient's blood pressure was 165 systolic

and 105 diastolic in the horizontal, 150 systolic and 100 diastolic in the sitting and 120 systolic and 75 diastolic in the standing position. The renal biopsy revealed grade 1 nephrosclerosis.

*Course.*—On Nov. 18, 1943 the patient was standing ten hours a day, as a postoffice clerk, behind the counter; the blood pressure of the patient in the horizontal position was 120 systolic and 80 diastolic, sitting 130 systolic and 90 diastolic and standing 130 systolic and 90 diastolic. The last follow-up, in October 1944, two years after operation, showed the patient at full work. The symptoms had disappeared. Blood pressure was 130 systolic and 70 diastolic in all three positions.

*Comment.*—This was a case of early hypertension, mostly systolic, with typical symptoms. The diastolic pressure of this patient only seldom reached 100 mm. The operation was not complete. (The chains were incompletely removed on either side.) There was no postural hypotension. The response of blood pressure to operation was not immediate, but a year and two years later the patient became asymptomatic and was at full work and his blood pressure was normal. This was a graded sympathectomy, with a good result up to date.

CASE 4 (table 3, case 13).—Margaret Z., a 21 year old unmarried woman, entered St. Luke's Hospital on June 15, 1941. With the exception of intermittent headaches, there were no complaints. One of these headaches was severe, lasted a whole day and was accompanied with nausea and vomiting. She had fallen from a horse several times; this was followed by dizziness for a day. There was some nycturia at times. She was rather highstrung, temperamental and readily upset.

*On Entrance.*—The patient's blood pressure was 160 systolic and 100 diastolic. The physical examination was noncontributory. The eyegrounds were normal. The heart occupied 40 per cent of the thorax. The electrocardiogram was normal. The urine was negative for pathologic elements. The intravenous pyelogram suggested a small and deformed left renal pelvis, but the retrograde pyelogram did not bear this out. The phenolsulphonphthalein excretion was 35 per cent in one hour; the urea clearance was 58 per cent (standard). Determinations of blood chemistry gave normal results. Sodium amytal depressed the blood pressure from 170 systolic and 104 diastolic to 135 systolic and 80 diastolic in millimeters of mercury. The cold pressor test raised it from 160 systolic and 100 diastolic to 190 systolic and 120 diastolic.

*Operations.*—Operations were done on June 26 and July 9, 1941, at which times a right and left splanchnic nerve section was done together with a dorsolumbar sympathectomy. Both chains were cut between the ninth dorsal and the second lumbar ganglion. The kidneys, ureters and adrenals were normal. A biopsy specimen taken from the right kidney revealed no pathologic changes.

*Course.*—The patient was discharged with blood pressures of 140 systolic and 80 diastolic, 120 systolic and 80 diastolic and 80 systolic and 0 diastolic in the three positions. The cold pressor response was minimal after the operation (140 systolic and 80 diastolic to 145 systolic and 80 diastolic). She continued to have occasional headaches but lived a healthy outdoor life, taking on the job of a wrangler on one of the western ranches. Her blood pressures fluctuated between 160 and 130 systolic and 100 to 80 diastolic during the next three years.

TABLE 5.—Results of Surgical Treatment of Hypertension (Grade 2)

| Case  | Patient | Age, Yr. | Pre-operative Blood Pressure | Eye-ground | Blood Pressure Under Sodium Amytal | Blood Pressure Under Vasoconstrictor | Post-operative Blood Pressure | Postural Hypotension | Symptoms                       | Working Ability | Period of Follow-up, Mo. | General Result, on Basis of 3 |
|---|---------|----------|------------------------------|------------|------------------------------------|--------------------------------------|-------------------------------|----------------------|--------------------------------|-----------------|--------------------------|-------------------------------|
| A. Males  |         |          |                              |            |                                    |                                      |                               |                      |                                |                 |                          |                               |
| 1   | L. F.   | 17       | 191/114                      | 1          | 165/100                            | 210/140                              | 145/90                        | 90/50                | None                           | 8 hr. day       | 22                       | 1                             |
| 2   | J. P.   | 25       | 180/120                      | 1          | 160/100                            | .....                                | 120/80                        | 85/40                | .....                          | Died            | 46                       | Died in mental institution    |
| 3   | J. A.   | 31       | 210/134                      | 2          | 140/110                            | 240/180                              | 145/105                       | 90/60                | None                           | .....           | 12                       | 1-2                           |
| 4   | M. W.   | 31       | 220/120                      | 2          | 138/96                             | 216/120                              | 150/130                       | 110/100              | Mild dizziness and palpitation | Good            | 8                        | 1                             |
| 5   | G. P.   | 33       | 200/130                      | 3          | 160/114                            | 172/120                              | 165/100                       | 102/88               | .....                          | .....           | ..                       | 2                             |
| 6   | E. Mc.  | 33       | 200/135                      | 1          | 156/120                            | 210/154                              | 170/110                       | 90/50                | .....                          | .....           | ..                       | 2                             |
| 7   | F. F.   | 33       | 200/120                      | 3          | 166/120                            | 210/122                              | 170/120                       | 116/110              | None                           | 8 hr. day       | 18                       | 2                             |
| 8   | J. T.   | 33       | 208/116                      | 3          | 150/80                             | 232/80                               | 162/110                       | 50/?                 | Dizziness and palpitation      | 8 hr. day       | 20                       | 1                             |
| 9   | G. R.   | 42       | 255/115                      | 3          | 170/90                             | .....                                | 160/100                       | 140/100              | None                           | 8 hr. day       | ..                       | 1                             |
| 10  | L. R.   | 44       | 230/150                      | 2          | 106/140                            | 234/190                              | 220/160                       | 84/76                | None                           | 8 hr. day       | 22                       | 2                             |
| 11  | R. F.   | 50       | 178/112                      | 1          | 144/88                             | 200/118                              | 150/90                        | 60/?                 | None                           | Good            | 15                       | 1                             |
| 12  | J. C.   | 51       | 230/130                      | 2          | 172/110                            | 238/156                              | .....                         | .....                | .....                          | .....           | ..                       | 2                             |
| 13  | J. F.   | 52       | 215/120                      | 2          | 142/92                             | .....                                | 236/124                       | 90/70                | None                           | 8 hr. day       | 14                       | 2                             |
| B. Females                                      |         |          |                              |            |                                    |                                      |                               |                      |                                |                 |                          |                               |
| 14  | M. W.   | 28       | 184/130                      | 1          | 154/98                             | 252/156                              | 170/102                       | 130/?                | Slight palpitation             | 8 hr. day       | 6                        | 1                             |
| 15  | K. deT. | 30       | 200/110                      | 2          | 166/118                            | 230/170                              | 140/110                       | 50/?                 | Some dizziness and palpitation | Fair            | 30                       | 2                             |
| 16  | L. T.   | 33       | 210/150                      | 1          | 130/110                            | 240/162                              | .....                         | 115/85               | .....                          | .....           | ..                       | 2                             |
| 17  | A. B.   | 33       | 180/110                      | 1          | 134/82                             | 180/115                              | 186/130                       | 138/80               | Headache                       | .....           | 30                       | 1                             |
| 18  | M. H.   | 34       | 200/120                      | 1          | 150/100                            | 250/150                              | 170/124                       | 165/100              | None                           | 8 hr. day       | 22                       | Unrelated symptoms            |
| 19  | A. M.   | 34       | 250/170                      | ..         | .....                              | .....                                | 280/130                       | 100/120              | .....                          | .....           | 9                        | 2                             |
| 20  | A. K.   | 34       | 190/120                      | 0          | .....                              | .....                                | 180/110                       | 150/98               | None                           | .....           | 22                       | 1                             |
| 21  | A. S.   | 39       | 220/140                      | 2          | 152/110                            | 225/135                              | 160/100                       | 100/70               | .....                          | .....           | ..                       | 1                             |
| 22  | M. D.   | 40       | 210/130                      | 1          | 172/120                            | 242/140                              | 182/110                       | 132/98               | .....                          | .....           | 17                       | 2                             |
| 23  | M. W.   | 46       | 160/118                      | 1          | 138/104                            | 170/100                              | 115/95                        | 94/?                 | Slight palpitation             | 8 hr. day       | 21                       | 1                             |
| Died; sudden collapse; autopsy non-contributory |         |          |                              |            |                                    |                                      |                               |                      |                                |                 |                          |                               |
| 24  | C. B.   | 45       | 256/150                      | 1          | 170/110                            | 280/164                              | 236/170                       | 108/78               | .....                          | .....           | ..                       | ..                            |

Postural hypotension had disappeared. In May 1944 she had a spell of unconsciousness, with a blood pressure of 90 systolic and 60 diastolic in millimeters of mercury, from which she temporarily recovered, but she died suddenly in a second attack, on May 28, 1944, not quite three years after operation. At autopsy (Dr. Foster and Dr. Hildebrand, Community Hospital, Geneva, Ill., No. 25270) no anatomic cause for death was found. The kidneys both grossly and microscopically were normal. Nothing was found in the brain.

*Comment.*—This is a case of nonrenal hypertension for which no cause could be found at autopsy. Note that a complete splanchnic section did not materially influence the blood pressure for the follow-up period of three years. This observation will be later discussed on the basis of other cases of "neurogenic" hypertension.

*Group 2.*—Twenty-four patients were available for study. This is a heterogeneous group in which organic vascular damage is definite, but vasomotor relaxation still produces a lowering of blood pressure, although not to a normal level. This group contains the group 2 and the earlier cases of group 3 of the Keith-Wagener classification. Operation has been definitely worth while in some and showed no result in others. Some patients have died, and the careful analysis of their histories has revealed some mistakes in indications or surgical technic (table 5). The ages of the patients in this group varied between 17 and 52 years; the preoperative blood pressure fluctuated between 256 and 160 systolic and 150 and 118 diastolic expressed in millimeters of mercury. The average preoperative blood pressure was 207 systolic and 128 diastolic in millimeters of mercury; this was depressed to an average of 176 systolic and 110 diastolic in millimeters of mercury, although in individual cases as low a level as 120 systolic and 80 diastolic could be reached. The average period of follow-up was 18.8 months, although a few patients have been followed as long as four years (table 6).

CASE 5 (table 5, case 1).—John P., a 25 year old punch press operator, was admitted to the Research and Educational Hospital, complaining of pain and ulceration of toes, blueness of fingers in both hands, dizzy spells and nervousness.

TABLE 6.—Summary of Results of Surgical Treatment of Hypertension (Grade 2) in Twenty-Four Cases

|              | Age, Years | Preoperative<br>Blood Pressure,<br>Mm. of Hg | Postoperative<br>Blood Pressure,<br>Mm. of Hg | Period of<br>Follow-up,<br>Months |
|--------------|------------|--|---|-----------------------------------|
| Maximum..... | 52         | 256/150                                      | 236/124                                       | 55                                |
| Minimum..... | 17         | 160/118                                      | 120/80  | 13                                |
| Average..... | 37.2       | 207/128                                      | 176/110                                       | 27.8                              |

*Past History.*—He was well until September 1939, when pain appeared in the right fifth toe. After heat and roentgen ray therapy, the skin broke down and

chronic ulcers developed. The patient lost his job. His fingers became cyanotic; he lost 35 pounds (16 Kg.) in the last year because of intractable pain in the extremities. There was angina pectoris on effort.

*On Entrance.*—The retinal vessels were narrow and tortuous and showed arteriovenous nicking. Blood pressure was 182 systolic and 122 diastolic in millimeters of mercury. The electrocardiogram showed myocardial damage. Urea clearance was 30.2 cc. per minute; the urea ratio was 44. Split kidney function showed delay in the appearance of the dye, chiefly on the left. Intravenous pyelograms were normal.

The distal phalanges of all fingers except the thumbs were cold and cyanotic; so were the toes. The left third toe had been previously amputated at the distal phalanx; the nail of the fourth toe had been removed and the fifth toe was gangrenous. A diagnosis of diffuse arteriolar disease with hypertension was made. Biopsy of muscle showed capillary stasis and arteriolar sclerosis. No evidence of periarteritis nodosa or thromboangiitis obliterans was found. The organic vascular damage was severe and diffuse.

*Operations.*—Operations were performed as follows: left and right cervico-dorsal sympathectomy on Nov. 11, 1939, left lumbar sympathectomy on Dec. 5, 1939, right lumbar sympathectomy with removal of a renal biopsy specimen on Jan. 23, 1940, left transdiaphragmatic splanchnic nerve section on Feb. 12, 1940, and right transdiaphragmatic splanchnic nerve section on Aug. 16, 1940.

*Course.*—The cyanosis, pain and ulceration of the extremities were relieved. The anginal pain disappeared. The blood pressure at first did not drop below 160 systolic and 100 diastolic in millimeters of mercury; however, with the patient in the erect position it was 85 systolic and 40 diastolic in millimeters of mercury. Standing still for five minutes produced dizziness; however, headaches and nervousness were relieved. Two months after operation the blood pressure was 115 systolic and 80 diastolic with the patient in the horizontal position and was inaudible in the vertical position. Amphetamine relieved the symptoms of postural hypotension. Four months after operation the horizontal and vertical pressures were almost the same. Six months postoperatively he was back at full work. Eight months after operation the blood pressure was 120 systolic and 80 diastolic in millimeters of mercury while the patient was lying down and 95 systolic and 70 diastolic in millimeters of mercury after he had stood for five minutes.

The histologic picture of the renal biopsy specimen (Dr. S. R. Rosenthal) revealed strikingly well preserved glomeruli, compared with the almost total destruction of tubules. These were replaced by dense fibrous tissue; rarely a tortuous dilated tubule was filled with casts. There was increase of fibrosis in the interstitial tissue, which was interspaced by numerous round cells. The latter formed nodules at focal points. The arterioles were greatly thickened as a result of intimal proliferation. The lumens were frequently completely obliterated or canalized. The arteries showed thickening of the intima and media but no obturation of the lumen. The impression was that of a secondary contracted kidney, probably a pyelonephritic kidney. Renal involvement was grade 3.

In spite of the almost complete sympathectomy (first to fourth dorsal and sixth dorsal to third lumbar ganglions on each side, with both major splanchnic nerves excised); there were motile spermatozoa in a fresh condom specimen.

This case has been previously reported by Helfrich and one of us.<sup>10</sup> The patient made repeated visits to the surgical dispensary; his blood pressure did not go above 130 systolic and 90 diastolic at any time. However, he began to show evidence of organic disease of the brain with dementia, although no acute episode occurred. He entered the Elgin State Hospital, where he died on Sept. 9, 1943. At autopsy (Dr. A. Lieberman) the significant findings were as follows: terminal hemorrhagic infarct in the left lower lobe of the lung and small, contracted kidneys with a fine mottled surface. Grayish brown areas of fibrosis alternated with hemorrhagic zones in the cut section. The renal arteries were patent. The heart showed an old infarction at the apex and a concentric hypertrophy. The brain appeared to be smaller than normal. There were a number of yellowish areas of softening, most pronounced in the left motor area. The left frontal lobe was unusually congested. There was a moderate degree of arteriosclerosis of the basal vessels. Histologic sections were not available to us for study.

*Comment.*—This was the case of a young man with severe diffuse arteriolar sclerosis of unknown origin. He certainly did not present the picture of a typical essential hypertension; in fact, his complaints were first related to the peripheral vessels. The renal biopsy, performed in 1940, was suggestive of pyelonephritis; yet three years later he did not die of malignant nephrosclerosis but of encephalomalacia. The patient, although the hypertension was relieved, had irreparable and progressive arteriolar damage and would not be considered operable under our present indications. Note that even an almost total sympathectomy is not capable of arresting the progress of this type of disease. It may have been due to lead intoxication or some other vascular poison.

**CASE 6.**—James T., a 39 year old farmer, was admitted to St. Luke's Hospital on March 19, 1942, complaining of severe occipital headaches for three years and progressive dyspnea on exertion for eight years. His heart palpitated occasionally. He was entirely incapacitated.

*Past History.*—The patient was well until eight years ago, when headache and dyspnea first developed. His blood pressure was not determined until six months ago, at which time it was 175 mm. of mercury (no doubt, systolic). There was no family history of hypertension and no history of renal disease in childhood.

*On Entrance.*—The patient's blood pressure was 208 systolic and 116 diastolic and varied at rest between 222 systolic and 135 diastolic and 176 systolic and 120 diastolic in millimeters of mercury. The eyegrounds revealed vasospastic retinopathy, with old hemorrhages and exudates, and a grade 3 fundus. The heart occupied 41 per cent of the thorax. An electrocardiogram revealed myocardial damage; there was some angina on effort. The basal metabolic rate was +7 per cent. The urine persistently contained albumin (4 plus); the phenolsulfonphthalein excretion was 15 per cent in fifteen minutes. The urea clearance was 29.2 cc. (standard); he concentrated urine to 1.020. On administration of sodium amytal his pressure dropped from 180 systolic and 120 diastolic to

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10. de Takats, G., and Helfrich, L. S.: Sterility of the Male After Sympathectomies, J. A. M. A. **117**:20 (July 5) 1941.



130 systolic and 80 diastolic; the cold pressor test revealed no rise. Epinephrine raised his pressure from 174 systolic and 94 diastolic to 232 systolic and 80 diastolic in millimeters of mercury. When his vascular status is sized up, the greatest damage seemed to be in the kidney and eyegrounds and less in the heart and peripheral vascular tree.

*Operations.*—Operations were performed on May 27 and June 15, 1942, at which times right and left transdiaphragmatic splanchnic nerve section and dorsolumbar sympathectomy from the ninth dorsal to the second lumbar ganglion were done. The renal biopsy revealed severe nephrosclerosis with narrow arteriolar lumens and hyaline changes in glomeruli and tubules. It was grade 3 nephropathy. The patient left the hospital with a blood pressure of 168 systolic and 92 diastolic, 130 systolic and 90 diastolic and 50 systolic and undetermined diastolic in the three positions. His postural dizziness and dyspnea were pronounced.

*Course.*—Although the patient lived in Arkansas, excellent follow-up records were obtained through the courtesy of Dr. L. L. Hubener. A year and a half after the operation his blood pressures were 160 systolic and 110 diastolic, 165 systolic and 110 diastolic and 150 systolic and 100 diastolic in the horizontal, sitting and standing positions. The pressure dropped to 135 systolic and 95 diastolic after exercise. He lost his headache and dizziness but had palpitation and was able to work full time except that he reported periods of incapacity, pointing to cardiac strain. The urine was concentrated to 1.020, with a faint trace of albumin and occasional pus cells. Two and a half years after operation he was living comfortably on a reduced physical schedule. His blood pressure varied from 165 to 150 systolic and 110 to 100 diastolic.<sup>10a</sup>

*Comment.*—This is a patient with severe organic damage but enough vasospasm so that the operation resulted in decided benefit. He was restored to a limited activity. His symptoms have subsided. It is doubtful whether his life expectancy has been greatly prolonged, but up to date, four years since the operation, his blood pressures have been lowered consistently and have not shown any tendency to rise.

*Group 3.*—Ten patients belong to this group (table 7). Their ages varied from 7 to 52 years. Their preoperative blood pressure varied from a maximum of 265 systolic and 155 diastolic to a minimum of 200 systolic and 170 diastolic, with an average of 234 systolic and 158 diastolic in millimeters of mercury. The average postoperative blood pressure was 210 systolic and 153 diastolic in millimeters of mercury, indicating no hypotensive effect. While there was no surgical mortality, all patients died within a year of the operation.

This is an extremely important group, since on the basis of our early experience with this type of patient we regard the patients in this group as entirely inoperable. The group includes not only patients in the malignant phase of hypertension but some of the late group 3 patients of the Keith-Wagener classification who have no papilledema and no necrotizing arterioles but who have retinal hemorrhages, poor

10a. Four years after operation, his blood pressure varied from 160 to 150 systolic and 110 to 100 diastolic.

TABLE 7.—Results of Surgical Treatment of Hypertension (Grade 3)\*

| Case       | Patient | Age, Yr. | Pre-operative Blood Pressure | Eye-grounds | Blood Pressure Under Sodium Amytal | Blood Pressure Under Vasconstrictor | Post-operative Blood Pressure | Postural Hypotension | Symptoms                  | Result | Period of Follow-up, Mo. | Autopsy  |
|------------|---------|----------|------------------------------|-------------|------------------------------------|-------------------------------------|-------------------------------|----------------------|---------------------------|--------|--------------------------|--|
| A. Males   |         |          |                              |             |                                    |                                     |                               |                      |                           |        |                          |  |
| 1          | F. P.   | 29       | 246/168                      | 3           | Not done                           | 246/168                             | 238/160                       | None                 | Hypertensive; uremia      | Died   | 4                        | Malignant nephrosclerosis                      |
| 2          | H. K.   | 52       | 247/140                      | 2           | 180/110                            | .....                               | Not operated on               | .....                | Vascular accident         | Died   | 4                        |  |
| B. Females |         |          |                              |             |                                    |                                     |                               |                      |                           |        |                          |  |
| 3          | S. S.   | 7        | 200/170                      | 4           | Not done                           | .....                               | 190/160                       | None                 | Same                      | Died   | 2                        | Congenital hypoplastic kidney                  |
| 4          | J. H.   | 7        | 240/190                      | 4           | 200/160                            | .....                               | Not operated on               | .....                | Uremia; vascular accident | Died   | 6                        | Malignant phase; congenital hypoplastic kidney |
| 5          | P. B.   | 7        | 225/160                      | 1           | Not done                           | .....                               | 180/150                       | .....                | Same                      | Died   | 2                        |  |
| 6          | B. H.   | 21       | 230/142                      | 4           | 230/142                            | .....                               | 210/140                       | None                 | Same                      | Died   | 2                        |  |
| 7          | E. H.   | 29       | 242/163                      | 2-3         | 214/160                            | 250/168                             | 200/160                       | 178/150              | Same                      | Died   | 2                        |  |
| 8          | C. S.   | 25       | 230/150                      | 4           | Not done                           | 230/150                             | Not operated on               | .....                | Same                      | Died   | 2                        |  |
| 9          | A. J.   | 39       | 265/155                      | 3           | 150/90                             | 250/170                             | Not operated on               | .....                | Same                      | Died   | 91                       | Not included in average                        |
| 10         | H. W.   | 27       | 230/140                      | 2           | 156/106                            | 250/147                             | 240/145                       | None                 | Same                      | Died   | ..                       | Not included in average                        |

\* In cases 1, 3 and 9 bilateral nephro-omentopexy was performed in addition to splanchnic section; in case 7 a nephrectomy was performed. Blood pressure as quoted is the average of maximum and minimum pressures obtained.

cardiac and renal reserve and fixed blood pressures, which hardly respond in any direction (table 8).

CASE 7 (not included in the tabulated series).—The history of case 7 was published in a previous communication.<sup>1</sup> Carmela S., a 25 year old married woman,

TABLE 8.—*Summary of Results of Surgical Treatment of Hypertension (Grade 3) in Ten Cases*

|              | Age, Years | Preoperative<br>Blood Pressure,<br>Mm. of Hg | Postoperative<br>Blood Pressure,<br>Mm. of Hg. | Period of<br>Follow-up,<br>Months   |
|--------------|------------|--|--|-------------------------------------|
| Maximum..... | 62         | 265/153                                      | 240/145  | All 10 died, 9                      |
| Minimum..... | 7          | 200/170                                      | 180/160  | within a year                       |
| Average..... | 24.3       | 234/158                                      | 210/153  | and 1 five years<br>after operation |

was admitted to St. Luke's Hospital on May 23, 1940, complaining of intractable headaches and vertigo of one year's duration.

*Past History.*—She suffered from mild headaches all her life. Four years previously, while pregnant, she was told of her high blood pressure. The delivery was uneventful, as she had been allowed to carry the baby to term, but two days after delivery eclampsia developed. The blood pressure never came down to normal. Aching in the eyeballs and headaches increased in severity. Two weeks before her entrance to the hospital, the patient became dizzy and fainted.

*On Entrance.*—Pronounced hypertensive retinopathy was found, with blurred disks, exudates and hemorrhages. The blood pressure varied from 230 to 210 systolic and 158 to 140 diastolic in millimeters of mercury. The heart was moderately enlarged to the left. The electrocardiogram showed myocardial damage. Renal function was poor, with a standard urea clearance of 15.3 cc. The urine contained less than 50 mg. of albumin but occasional red cells. There was no nitrogenous retention. The intravenous pyclogram was normal. The responses to cold, to epinephrine and to sodium amytal were slight. A diagnosis of post eclamptic hypertension terminating in malignant nephrosclerosis was made. Operation was not advised.

*Course.*—The intractable headaches were not influenced by irradiation of the pituitary. Sudden death occurred two months after discharge, presumably from massive intraventricular hemorrhage. Autopsy was not done.

*Comment.*—There can hardly be any doubt that such a patient cannot be benefited by operation, and there is fair unanimity among surgeons that such patients are inoperable. All our patients belonging to this group died; our attempts at a revascularization of the kidney by implanting omentum or muscle have equally been unsuccessful.<sup>9</sup>

CASE 8 (case 6 in table 7).—Betty H., a 21 year old married woman, entered the Research and Educational Hospitals on Nov. 2, 1939, complaining of severe continuous headache, nausea, vomiting and severe pain in the chest lasting for two weeks.

*Past History.*—She was well up to the age of 17, when four months after being married she had a miscarriage. Her physician told her that she would never have a full term baby. A few months later she again became pregnant; she was told of her high blood pressure and albumin in the urine. Her feet

were swollen. Labor was induced, and she was unconscious for two days. A year later she had continuous headaches and then again became pregnant. She lost this baby around the third month. After this, nausea and vomiting were frequent. In April 1939 paralysis of the right facial nerve occurred, and in September 1939 paralysis of the left facial nerve developed. Severe knifelike pain appeared under the left costal margin. She did not know whether her pressure fell or not during this time.

*On Entrancce.*—Both eyegrounds showed papilledema, exudates and hemorrhages. Blood pressure varied from 250 to 210 systolic and from 150 to 136 diastolic in millimeters of mercury. Neither pentothal sodium given intravenously nor sodium nitrite or sodium amytal administered orally were able to depress the diastolic pressure below 140 mm. of mercury. Potassium thiocyanate was ineffective. Renal function was greatly impaired, the urea clearance being depressed to 15 cc. per minute but with no nitrogenous retention. The urine showed red blood cells and casts, with 0.2 to 1.4 Gm. of albumin daily. The heart was enlarged, and the electrocardiogram showed evidence of myocardial damage.

*Operations.*—Operations on Jan. 2 and Jan. 23, 1940 consisted of bilateral supradiaphragmatic section of the splanchnic nerves. On discharge the blood pressure had reached its preoperative level. She died at home, suddenly, two months later.

*Comment.*—The past history of this young woman is pitiful. She should have been sterilized after her first miscarriage because of the toxemic hypertension. As will be discussed later, our results in patients with post-toxemic hypertension have been favorable when the original vascular injury does not repeat itself. In this patient three pregnancies produced, in the course of four years, malignant nephrosclerosis. We operated on some patients of this type four to five years ago, on the plea of the internists that they are young, that they resist medical treatment and that they are otherwise lost. Our experience has been that no type of operation, whether extensive splanchnic section or muscle transplants to the kidney, can save such patients. This stage should be regarded as contraindicating operation.

While there is fair agreement about the malignancy and intractability of hypertension in such patients, we wish to present another group in whom we have been unable to modify the course of the disease and who therefore have not been subjected to operation in the last few years.

CASE 9.—John F., a 52 year old switchman, entered St. Luke's Hospital on Sept. 13, 1942, complaining of dizzy spells, headaches and palpitation. He had known of his hypertension for six years.

*Past History.*—A doctor discovered that the man had high blood pressure six years ago, but the patient was asymptomatic at the time. Two years ago a diagnosis of essential hypertension was made, and the patient was given potassium thiocyanate. Under this drug the lowest blood pressure obtained was 150 systolic and 90 diastolic in millimeters of mercury. The blood pressure in the right arm was persistently 15 to 20 mm. of mercury lower than that in the left arm. In the past few months the symptoms have been severer.

*On Entrance.*—The patient's blood pressure was 226 systolic and 130 diastolic in millimeters of mercury. The eyegrounds revealed a mild narrowing of the retinal arteries, with pronounced nicking of the veins. The heart occupied 40 per cent of the thorax. The thoracic aorta was tortuous and calcified. An electrocardiogram revealed mild myocardial damage. An intravenous pyelogram was normal. He concentrated urine between 1.002 and 1.020; the urea clearance was 53.1 cc. (standard). Under administration of sodium amytal the pressure in the right arm fell from 182 systolic and 110 diastolic to 156 systolic and 90 diastolic. In the left arm it fell from 230 systolic and 130 diastolic to 142 systolic and 92 diastolic.

*Operations.*—Operations were done on Sept. 21 and Oct. 24, 1942. During the first stage an epiglottic retention cyst was removed, which was discovered on intubation. The second stage was followed by a stormy course. On the third postoperative day the patient had an attack of severe retrosternal pain, dyspnea and cyanosis; the blood pressure dropped to 80 systolic and 60 diastolic in millimeters of mercury. The patient responded well to our routine therapy for pulmonary embolism; this diagnosis was considered most likely, since the electrocardiogram revealed minimal changes from the preoperative one. The patient left the hospital with pressures of 170 systolic and 100 diastolic, 180 systolic and 100 diastolic and 90 systolic and 70 diastolic in millimeters of mercury in the three positions. Renal biopsy revealed grade 1 nephrosclerosis.

*Course.*—A year after the operation, the patient's blood pressure was 236 systolic and 124 diastolic in the sitting and 222 systolic and 120 diastolic in millimeters of mercury in the standing position. He worked eight hours daily for the railroad and was free of dizziness or headaches. He was short of breath on climbing stairs. Otherwise he felt fine. Two years after operation a note was received from California, stating that he had an office job and was free of symptoms. The patient's blood pressure on the right was 170 systolic and 110 diastolic in the sitting position.

*Comment.*—This is the case of a middle-aged man who when entering the hospital exhibited grade 1 hypertension; he showed a satisfactory drop on administration of barbiturates. However, there was evidence of arteriosclerosis in the major arteries, notably in the aorta. He had a calcified plaque near the origin of the right subclavian artery, and the aortic knob was large and calcified. Nephrosclerosis in this type of patient is moderate and progresses slowly. The operation obviously does nothing to remedy the arteriosclerosis of the major vessels. It is true that he became asymptomatic, but rest and change to an easier job would have done this for him. Having observed a small group of such arteriosclerotic hypertensive patients postoperatively, we have come to the conclusion that they are not noticeably benefited from the operation. However, attention will be called later to the redistribution of effective blood volume which occurs in all patients with complete splanchnic section and which relieves some of their symptoms; it may also be responsible for ischemic symptoms in the brain and heart, since dizziness, blindspots or relative coronary insufficiency can occur in these patients. We have placed them in this third

group of nonoperable patients, although on mechanical grading they belong to the first group. Evidence of arterial and arteriolar sclerosis of degenerative nature is the dominant feature in this group. This is not to be confused with the hyperplastic arteriolar sclerosis and productive endarteritis which is seen in some of the toxic and inflammatory renal lesions leading to hypertension.

*Special Subgroups.*—All classifications of hypertension contain a differentiation between a nonrenal and a renal type of hypertension. It is generally assumed that the case of the so-called neurogenic type of hypertension is the ideal case for splanchnic nerve section. In fact, an effort has been made to differentiate the neurogenic from the renal hypertension by the response of the patient's blood pressure to high spinal anesthesia, since presumably the patient with the neurogenic type would be the one to operate on.<sup>11</sup> In addition, Grimson and his

TABLE 9.—*Classification of Patients Suffering from "Essential" Hypertension*

| Nonrenal                      | Number of Patients |    |
|-------------------------------|--------------------|----|
| "Neurogenic".....             | 3                  |    |
| Endocrine.....                | 2                  |    |
| Atheromatous.....             | 3                  |    |
| Total number.....             | —                  | 8  |
| Renal                         |                    |    |
| Unilateral renal disease..... | 4                  |    |
| Renal trauma.....             | 2                  |    |
| Toxemia of pregnancy.....     | 6                  |    |
| Pyelonephritis.....           | 3                  |    |
| Scarlet nephritis.....        | 5                  |    |
| "Rheumatic kidney".....       | 3                  |    |
| Total number.....             | —                  | 23 |
| Unclassified—19               |                    | 50 |

co-workers have proposed total sympathectomy in man because in their experimental neurogenic hypertension, produced by section of the buffer nerves, more limited procedures, such as splanchnic nerve section and dorsolumbar sympathectomy, were of little avail.<sup>12</sup>

Our experience, however, has not supported the view that the patients with nonrenal hypertension do better after operation than the patients with definable renal lesions. In our series an attempt has been made to define these groups, so that a comparison of results can be made between them (table 9). Naturally the extent of vascular damage,

11. Page, I. H.; Taylor, R. D.; Corcoran, A. C., and Mueller, L.: Correlation of Clinical Types with Renal Function in Arterial Hypertension: II. Effect of Spinal Anesthesia, *J. A. M. A.* **124**:736 (March 11) 1944. Page, I. H.: Certain Aspects of the Relationship Between Hypertension and Anesthesia, *Anesth. & Analg.* **22**:196, 1943.

12. Grimson, K. S.: Total Thoracic and Partial to Total Lumbar Sympathectomy and Celiac Ganglionectomy in Treatment of Hypertension, *Ann. Surg.* **114**:753, 1941.

as developed in the previous grading, has a potent influence with the groups.

#### THE RENAL BIOPSIES

The technic of performing a renal biopsy, a simple procedure which prolongs the operation by only a few minutes, has already been described. We have omitted it only in patients in whom because of severe hypotension or a large pneumothorax it was thought advisable to terminate the operation as soon as possible.

In an attempt to revascularize the ischemic kidney by omental or muscular grafts, Scupham and one of us (G. de T.) illustrated the value of cortical specimens taken from the kidney in 1940. We were stimulated to use this method of study by the excellent work of Chabanier and his co-workers,<sup>13</sup> who pointed out the difficulty of interpreting a late histologic picture, and to determine whether it is primarily vascular with secondary nephritic changes or primarily inflammatory with secondary vascular changes. Since 1939 we have taken sixty-five renal biopsy specimens, overwhelmingly from only one side, since with the exception of a few cases of unilateral renal disease the lesion was bilateral and differed little if at all on the two sides.

In the meantime the excellent correlation of clinical studies and renal specimens was presented by Smithwick and his co-workers.<sup>14</sup> They established the fact that the severer the renal vascular disease the more reduced were the glomerular filtration rate and the renal blood flow. They also found that constriction of the efferent glomerular arterioles as represented by the filtration rate was not present in the early stages of renal vascular disease. Finally they emphasized the finding that clinical hypertension and its grades of severity were ahead of the microscopic changes. In other words, hypertension seemed to precede renal vascular disease, which seemed secondary to it.

Our microscopic studies, undertaken at various periods between 1939 and 1945, were made by Dr. S. R. Rosenthal. Dr. Edwin F. Hirsch and the late Dr. Richard M. Jaffé. They have been restudied and reclassified by one of us (R.J.J.). Dr. Granville R. Bennett offered

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13. Chabanier, H.; Gaume, P., and Lobo-Onell, C.: *Vue d'ensemble sur les résultats d'interventions pratiquées dans quarante-neuf cas de néphroangioscléroses*, *Presse méd.* **46**:1818, 1938.

14. (a) Castleman, B.; Smithwick, R. H., and Palmer, R. S.: *Renal Biopsies from Hypertensive Patients*, *Am. J. Path.* **17**:617, 1941. (b) Talbot, J. H.; Castleman, B.; Smithwick, R. H.; Melville, R. S., and Peeora, L. J.: *Renal Biopsy Studies Correlated with Renal Clearance Observations in Hypertensive Patients Treated by Radical Sympathectomy*, *J. Clin. Investigation* **22**:387, 1943. (c) Castleman, B., and Smithwick, R. H.: *The Relation of Vascular Disease to Hypertensive State Based on Study of Renal Biopsies from One Hundred Hypertensive Patients*, *J. A. M. A.* **121**: 17) 1943.

valuable counsel. We have also studied the juxtaglomerular apparatus in some cases, with the help of Dr. E. D. Lambert, but have not found it to be of any help in the problems involved.

An intensive study of thirty renal biopsy specimens was made. We have used the terminology of Moritz and Oldt in describing vascular changes, recognizing subintimal hyalinization, medial hypertrophy and endothelial hyperplasia with reduplication of the internal elastic membrane. The material has been grouped into five classes similar to the scheme of Castleman and Smithwick.<sup>14</sup> A table of degree of changes observed follows:

| Grade  | Number of<br>Biopsy Specimens | Per Cent  |
|--------|-------------------------------|-----------|
| 0..... | 2                             | 6.6       |
| 1..... | 9                             | 30        |
| 2..... | 9                             | 30        |
| 3..... | 6                             | 20        |
| 4..... | 4                             | 13        |
|        | <hr/> 30                      | <hr/> 100 |

The two biopsy specimens which showed no vascular changes were from 1 patient with group 1 hypertension. Glomerular structures, interstitial tissue and tubules were without change. The biopsy specimens classified as group 1 demonstrated beginning subintimal hyalinization of scattered arterioles, and occasionally vessels over 100 microns in diameter revealed slight thickening of the media, although only a few were affected. There was an occasional narrow wedge-shaped area of fibrosis, and one or two glomeruli were completely scarred (fig. 8).

In group 2 the changes were more advanced and the vessels were immediately more conspicuous. The subintimal hyalinization was prominent in the involved arterioles and was present as a thick complete collar of pink-staining material. Furthermore, in vessels over 100 microns in diameter, beginning reduplication of the internal elastic membrane was apparent. Usually more glomeruli were hyalinized and focal infiltration of round cells was seen (fig. 9).

The six biopsy specimens classified as group 3 revealed involvement of almost all vessels. The arterioles contained hyalin rings of varying thickness, and in several of the larger arterioles and smaller arteries reduplication of the elastica was prominent. In others hypertrophy of the media was present. In this group distinct narrowing of the lumens by encroachment of thickened vessel walls was clearly seen. In some, sizable wedge-shaped areas of fibrosis and cellular infiltration were present (fig. 10).

In the last group every vessel was involved and the narrowing of the lumens, observed in the previous class, had advanced to almost complete obliteration in many instances. Hyalin could be seen in many of the arterioles, but others demonstrated pronounced intimal prolifera-



tion and elastic reduplication, with narrowing of the orifices to mere slitlike openings. In 1 case necrosis of the afferent arteriole and glomerulus was observed, and this was considered as an example of so-called malignant nephrosclerosis. In these biopsy specimens the interstitial scarring was not so pronounced as that in the previous group,

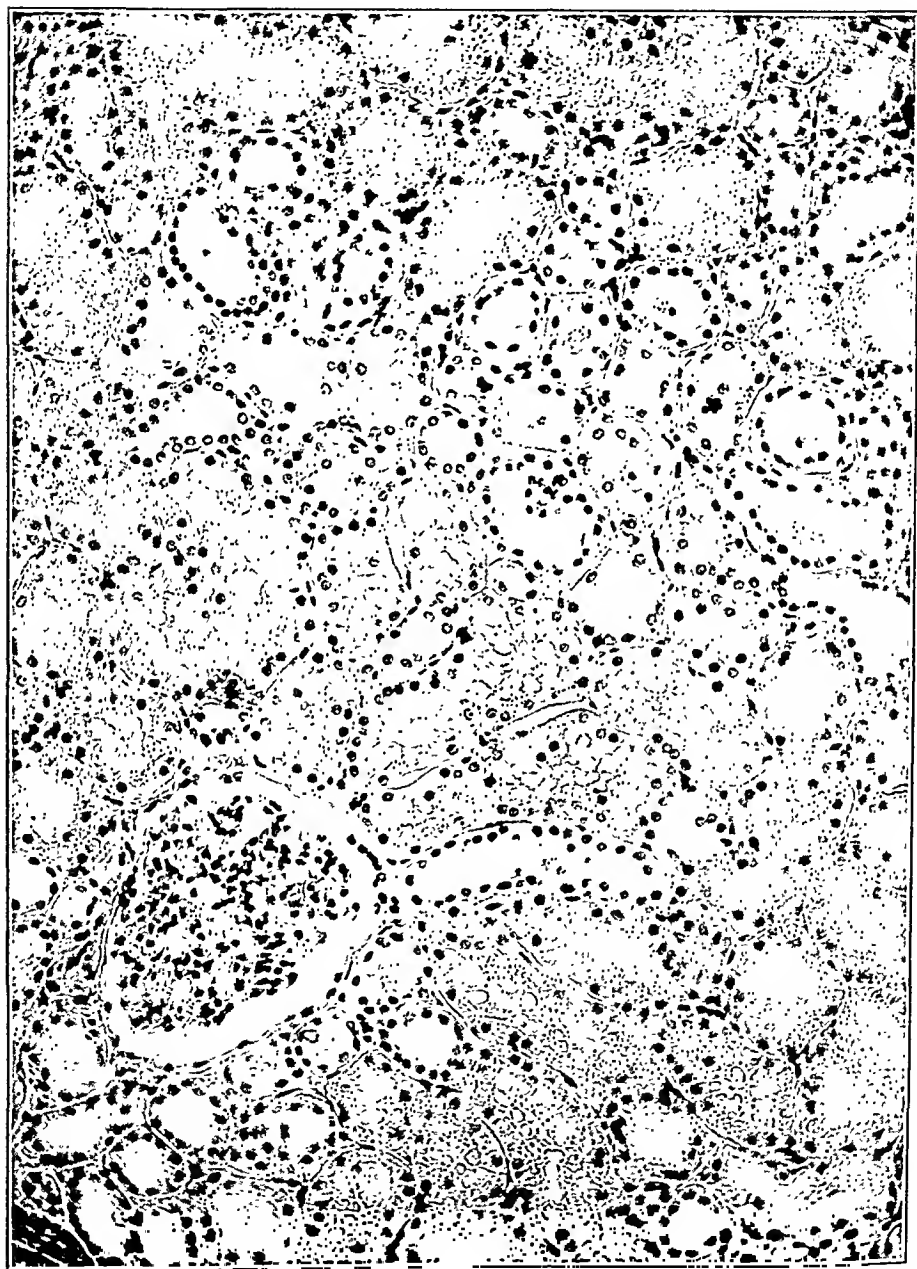


Fig. 8.—Vascular changes, group 1. There are essentially normal glomerulus and tubules. One arteriole above the tuft shows beginning hyalinization.

suggesting a more rapid tempo to the arterial and arteriolar changes (fig. 11).

From the pathologic standpoint, the first three groups constitute over 60 per cent of the cases. In these the vascular changes at most are

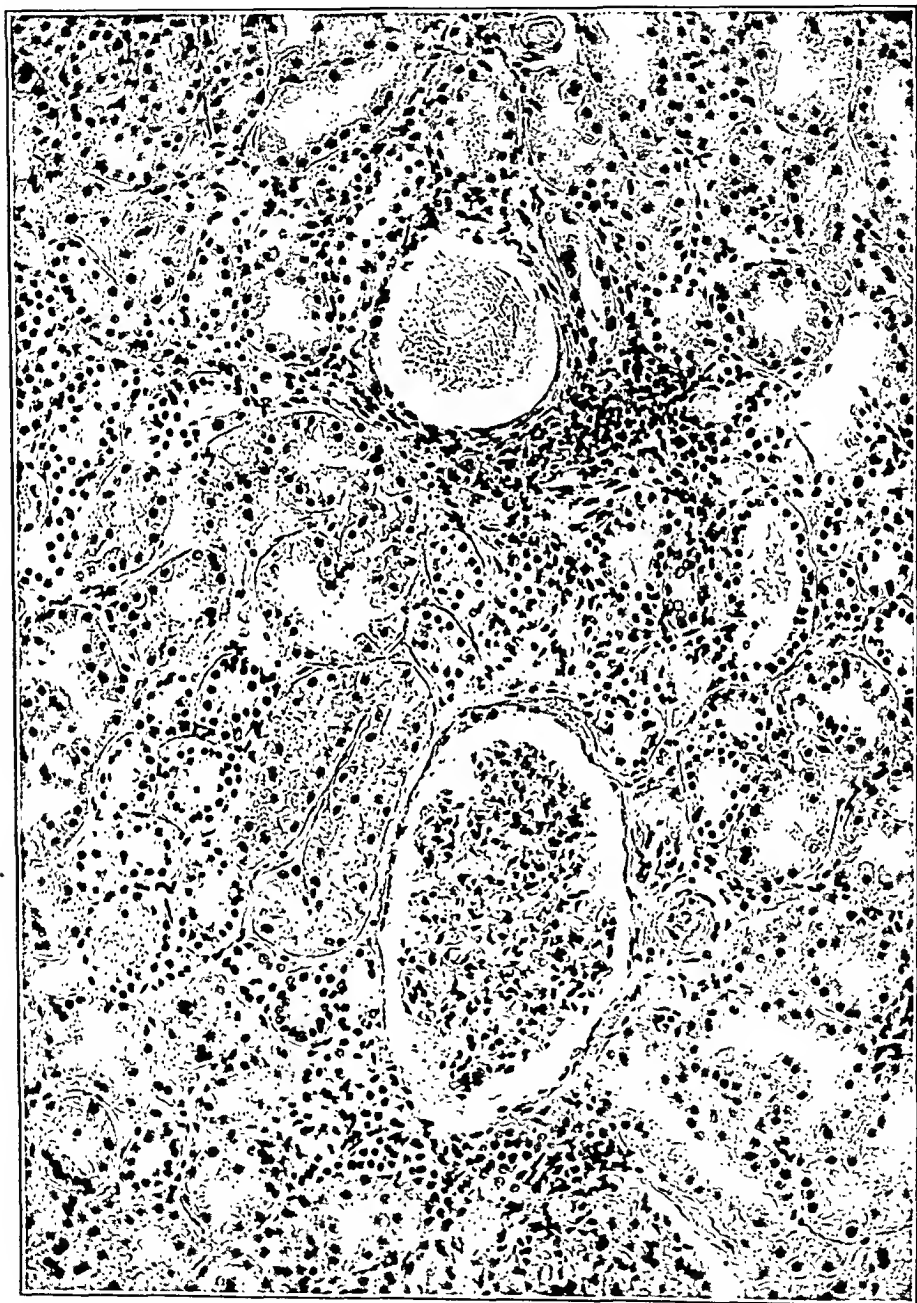


Fig. 9.—Vascular changes, group 2. Two arterioles below the glomerulus demonstrate more pronounced hyalinization. There is slight scarring and round cell infiltration of interstitial tissues.

minimal in character. Only in the latter two are the advanced changes apparent which are frequently encountered in necropsy material. Although this series is small, it is of especial interest to see that in these patients having hypertension over prolonged periods vascular changes in over 60 per cent are still within normal limits. This is further supportive evidence of the conclusion of Smithwick and Castleman that the hypertensive state antedated the vascular change.

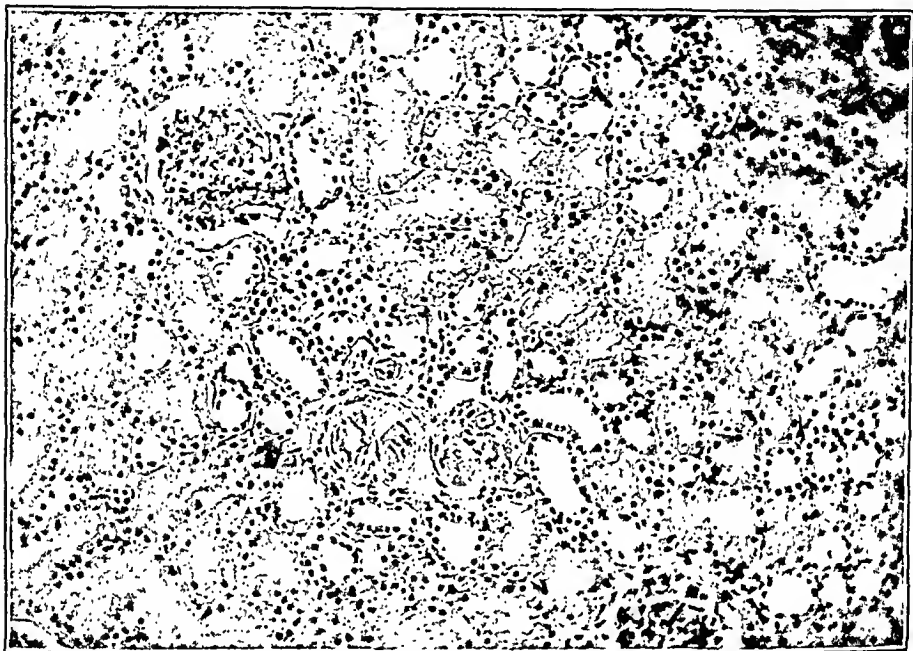


Fig. 10.—Vascular changes, group 3. The arterioles are more prominent and demonstrate subintimal hyalin and splitting of the internal elastic membrane.

The main question to be answered is, briefly, this: What information can the renal biopsy furnish toward the better understanding of the individual case? The second question is this: Does it have more prognostic value than the clinical study and the biopsies of muscle?

One of our earliest biopsies revealed chronic pyelonephritis in a young girl who gave the clinical picture of juvenile essential hypertension. Since a differential diagnosis between pyelonephritis and nephrosclerosis is important in this connection and since pathologists are more familiar with the end stages of the disease on the postmortem table, we are presenting a table based on the monograph of Weiss and Parker<sup>15</sup> (table 10). It will be noted that this table does not consider

15. Weiss, S., and Parker, F., Jr.: Pyelonephritis: Its Relation to Vascular Lesions and to Arterial Hypertension, *Medicine* 18:221, 1939.

the behavior of the glomeruli, tubules and interstitial tissue and is concerned only with the vascular system.

This differentiation between inflammatory and degenerative changes, however, also holds for other renal vascular lesions, such as we

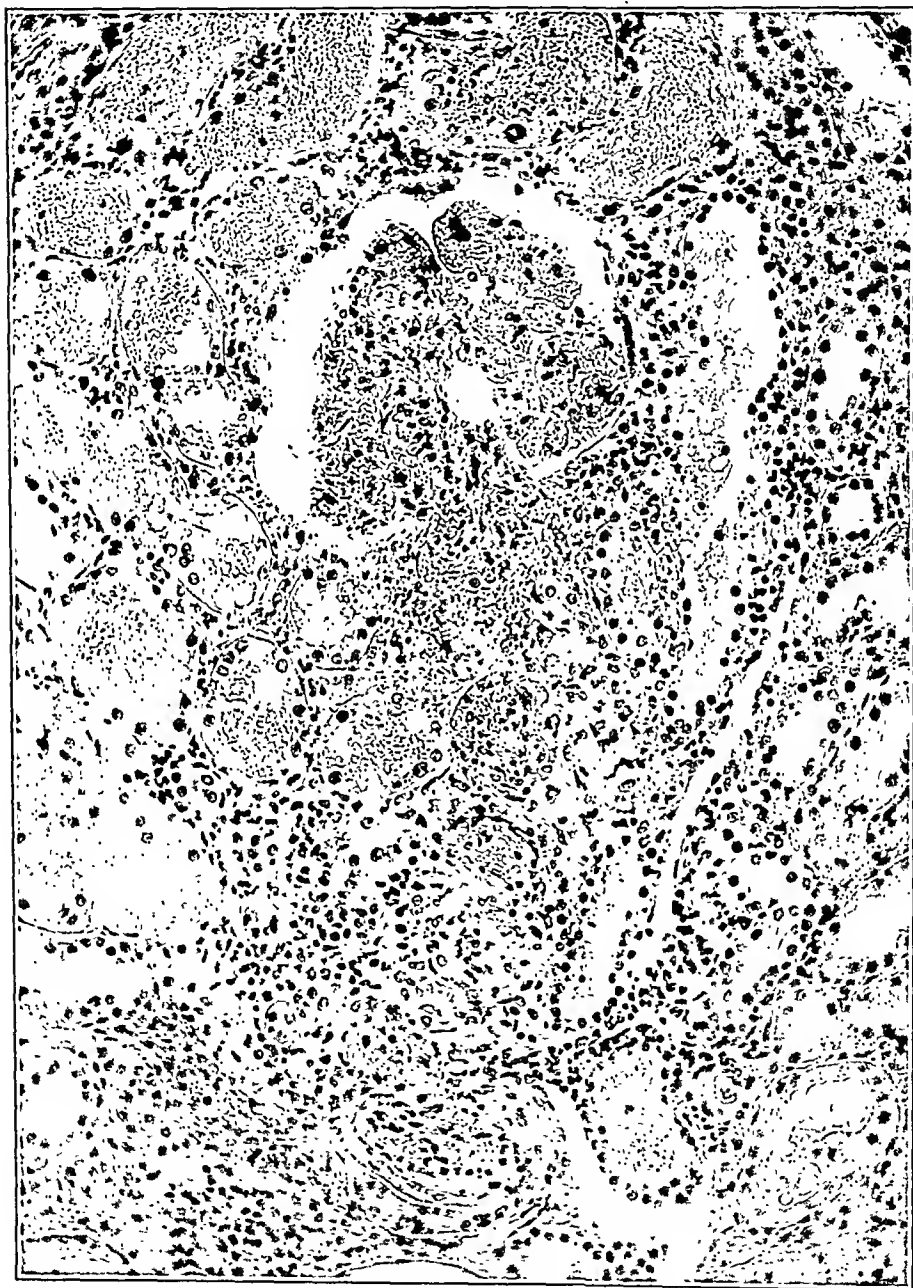


Fig. 11.—Vascular changes, group 4. The kidney in a case of malignant nephrosclerosis. There is necrosis of the tortuous afferent arteriole and the glomerular tuft.

encountered in glomerulonephritis, in streptococcic nephritis, in rheumatic lesions and in lesions accompanying Buerger's disease and panarteritis nodosa. Its significance lies in the fact that while nephrosclerosis seems to be the result of hypertension and is a secondary vascular lesion the inflammatory vascular lesions are primary in the kidney and are followed by hypertension.

Obviously, in later stages of the disease, in which nephrosclerosis is superimposed on an old inflammatory lesion, both lesions are con-

TABLE 10.—*Differential Diagnosis of Vascular Lesions in Pyelonephritis and Nephrosclerosis\**

| Vascular Lesion In | Pyelonephritis   | Nephrosclerosis †   |
|--------------------|--|---|
| Arteries           | Productive endarteritis (basophilic reticular tissue); reduplication of internal elastic membrane; medial hypertrophy                        | Internal thickening due to acidophil, dense connective tissue and hyalinization; splitting and reduplication of the internal elastic membrane |
| Arterioles         | Concentric proliferation of cells with increase in collagen; hyperplastic arteriolar sclerosis; hyaline degeneration only in the older group | Hyaline degeneration  |

\* Based on the monograph of Weiss, S., and Parker, F., Jr., *Medicine* 18:221, 1939.

† The malignant phase produces changes identical with those seen in pyelonephritis, i. e., productive endarteritis and hyperplastic arteriolar sclerosis.

comitantly present and it may be difficult to establish the priority of one over the other. It is also clear that different infections or toxic or allergic factors acting on the renal vascular bed will present the same proliferative reaction unless caught in the acute phase. This is equally true of the peripheral vascular bed in cases of thromboangiitis obliterans, panarteritis nodosa or rheumatic arteritis in which the characteristic picture is frequently absent when biopsies are performed during the chronic or healed stages. In our material, patients have been studied suffering from Buerger's disease, lupus erythematosus or streptococcic infections who exhibited hypertension and an inflammatory vascular reaction in the kidney without permitting a specific diagnosis.

One can state, then, that the differentiation of a primary inflammatory or secondary degenerative vascular lesion ought to be possible, especially in the earlier cases in which these biopsy specimens originate. The second problem is whether or not the renal biopsy performed during the first stage of the two stage procedure gives any prognostic help and whether it may modify the surgical procedure of the second stage. Examples of this type can be illustrated by the cases of L.T.B. and L.C.; both of these patients showed such severe renal changes and their

reaction to the first stage was so poor that the second stage was never carried out.

When an attempt was made to correlate the clinical grading with the grading of the histologic sections, as undertaken by Castleman and his co-workers,<sup>14</sup> their contention that the clinical grades are generally more advanced than the renal histologic changes was thoroughly substantiated. Table 11 summarizes our findings.

Another question arises regarding the comparative value of biopsies of muscle and whether or not such biopsies, performed during the pre-operative work-up or during the first stage of the operation, would be

TABLE 11.—*Correlation of Clinical Grades of Hypertension with Renal Histology*

| Grades | Number of Cases |       | Comment  |
|--------|-----------------|-------|--|
|        | Clinical        | Renal |  |
| 1      | 10              | 14    | Four patients with grade 2-3 hypertension had grade 1 renal changes  |
| 2      | 13              | 9     | Four patients differed, the biopsy specimens always showing less advanced changes  |
| 3      | 7               | 7     | One patient with malignant hypertension had a grade 1 renal biopsy specimen; 1 grade 2 patient showed grade 3 histologic changes |

an adequate substitute for renal biopsies. Heyer and Keeton,<sup>16</sup> from our institution, studied fifty-three specimens from skeletal muscle of hypertensive patients and concluded that regardless of the origin of the hypertension the histologic changes were the same: hypertrophy of the medial layer, constricting the lumen and altering the lumen to wall ratio. Only in the group with acute glomerulonephritis was the wall to lumen ratio slightly below that of the normal group. Once a pathologic lumen to wall ratio was established this was irreversible, since it did not change after a sympathectomy even though the pressure returned to normal. It is obvious, then, that, as first brought out by Kernohan, Anderson and Keith,<sup>17</sup> the hypertension can be graded and clinically correlated by the help of biopsy specimens taken from skeletal muscle. Nothing can be said, however, about the origin of hypertension, whereas the renal biopsy may here furnish more definite information.

Foa, Foa and Peet<sup>18</sup> stated on the basis of three hundred and fifty biopsies of muscle that they correlate well with blood pressure readings,

16. Heyer, H. E., and Keeton, R. W.: Arteriolar Changes of Skeletal Muscle in Patients with Hypertension of Varied Origin, *Am. J. Clin. Path.* **11**:818, 1941.

17. Kernohan, J. W.; Anderson, E. W., and Keith, N. M.: The Arterioles in Cases of Hypertension, *Arch. Int. Med.* **44**:395 (Sept.) 1929.

18. Foa, P. P.; Foa, N. L., and Peet, M. M.: Arteriolar Lesions in Hypertension: A Study of 350 Consecutive Cases Treated Surgically; an Estimation of the Prognostic Value of Muscle Biopsy, *J. Clin. Investigation* **22**:727, 1943.

changes in the eyegrounds and postoperative results. They suggest routine biopsies of muscle.

Our experience with biopsies of muscle has been that unless careful micrometer measurements are made by the same person nothing more than luminal constriction can be diagnosed; the methods of fixation and the site of the biopsy specimen may influence the wall to lumen ratio. Since we use a pedicled muscle flap to cover the renal defect, a small specimen of muscle is always obtained, more for purposes of record than for any help that it offers.

We have not been able to secure any renal biopsy specimens several months or years after splanchnic nerve section to compare them with the preoperative picture. As we pointed out in a previous communication, there was no observable change after muscle or omental transplants. While it is hard to imagine that glomeruli could be revascularized, tubular revascularization and hypertrophied tubular function which occur during the course of repair in man<sup>19</sup> might be facilitated. However, as will be discussed under the heading of general comment, the beneficial effect of splanchnic nerve section, at least in part, is extrarenal.

#### SPECIAL POSTOPERATIVE STUDIES

The purpose of dorsolumbar sympathectomy and splanchnic nerve section is to lower the blood pressure of hypertensive patients to a normal or at least a lower and more stable basal level. However, other observations can be made to substantiate the value and clarify the mechanism of such operations.

*The Eyegrounds.*—During our earlier studies photographs of fundi were taken at the Research and Educational Hospitals by Dr. T. Riser of all patients before and after splanchnic nerve section.<sup>20</sup> The regression of papilledema is striking in the group of patients with malignant hypertension, but it has no prognostic significance, since the patient still dies within the first year. The papilledema may recede even if systemic arterial blood pressure hardly falls, indicating that venous pressure and spinal fluid pressure are instrumental in its maintenance. This would fit with our conception that splanchnic section acts like an intermittent venisection, since the blood depots fill up and less of the blood volume circulates.

Papilledema and extensive retinal hemorrhages have caused us to reject the patient for operation, since they indicate malignant or pre-

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19. Oliver, J.: *Architecture of the Kidney in Chronic Renal Disease*, New York, Paul B. Hoeber, Inc., 1939.

20. Scientific Exhibit, American Medical Association, 1942.

malignant vascular damage. Occasionally the administration of ascorbic acid and of vitamin P (hesperidin) may improve the retinal status, but the dominant factor in the production of retinal vascular sclerosis is the height and duration of arterial hypertension. The diabetic hypertensive patient has a type of venous thrombosis with secondary hemorrhage which usually accompanies the peripheral neuropathy of diabetic patients<sup>21</sup> and which seems to have no relation to high blood pressure.

Vasospastic retinopathy which is seen with or without general hypertension requires careful ophthalmologic study. The study of Gifford and Marquardt is recommended in this connection.<sup>22</sup>

Since the study of the retina allows a certain insight into the status of cerebral circulation, 1 patient in whom a partial amblyopia developed following operation needs special mention.

Mrs. A. R., a 50 year old woman with hypertension grade 2, had bilateral splanchnic nerve section done on Aug. 25 and Sept. 26, 1944. Her preoperative retinal study showed grade 2 arteriosclerotic retinopathy. Her preoperative blood pressure was 230 systolic and 164 diastolic to 200 systolic and 150 diastolic. On September 29, three days after the completion of the second stage, the patient complained of a kidney-shaped spot in the field of vision. It was located a short distance to the right of the fixation point. No lesion was found in the eyegrounds, although the right macula looked a bit anemic. The blood pressure was 170 systolic and 130 diastolic in millimeters of mercury. The patient was followed in the eye dispensary. Seven months after operation, her blood pressure was 180 systolic and 110 diastolic. She still had a persistent black spot in front of her right eye. This must have been due to a focal cerebral ischemia.

*The Roentgenograms of the Chest, Taken at a Distance of 2 Meters.*—The cardiothoracic diameter and the size and shape of the aorta were noted before and after operation. The decrease in the size of the heart may be striking, and it occurs so shortly after operation that it must be due to decrease of intracardiac tension, or, in other words, to a lessening of cardiac hypertrophy, even if blood pressure is not significantly lowered. The heart of an athlete remains enlarged long after the initial physical strain; the heart of a hypertensive patient shrinks shortly after the lowering of blood pressure (fig. 12).

*The Electrocardiograms.*<sup>23</sup>—What is true of the size of the heart after operation seems to apply to the electrocardiogram. Four pairs of electrocardiograms are shown. The first electrocardiogram in each pair represents a preoperative tracing, and the second electrocardiogram in

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21 Rundles, R. W.: Diabetic Neuropathy, *Medicine* 24:111, 1945.

22. Gifford, S. R., and Marquardt, G.: Central Angiospastic Retinopathy, *Arch. Ophth.* 21:211 (Feb.) 1939.

23. Dr. G. K. Fenn described and interpreted the electrocardiograms.



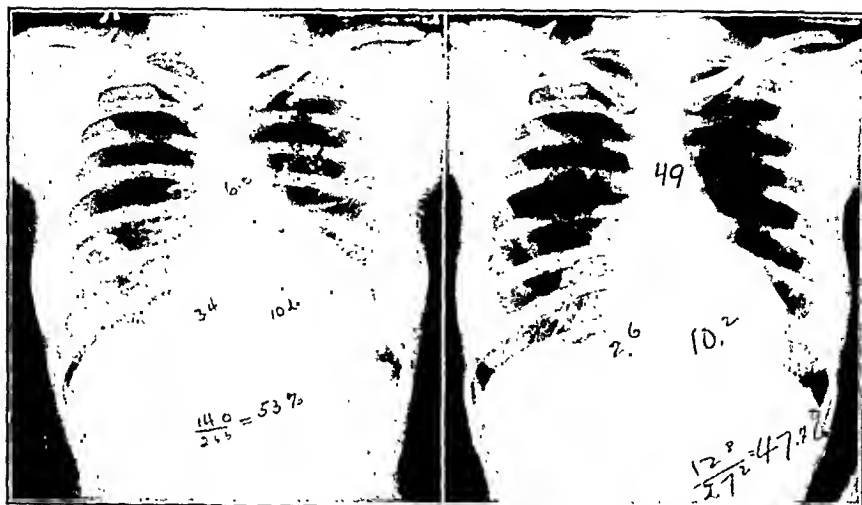


Fig. 12.—Roentgenograms of the chest taken at a distance of 2 meters before and two years after splanchnic nerve section for hypertension. Note that not only the size of the heart but the width of the large vessels has decreased.

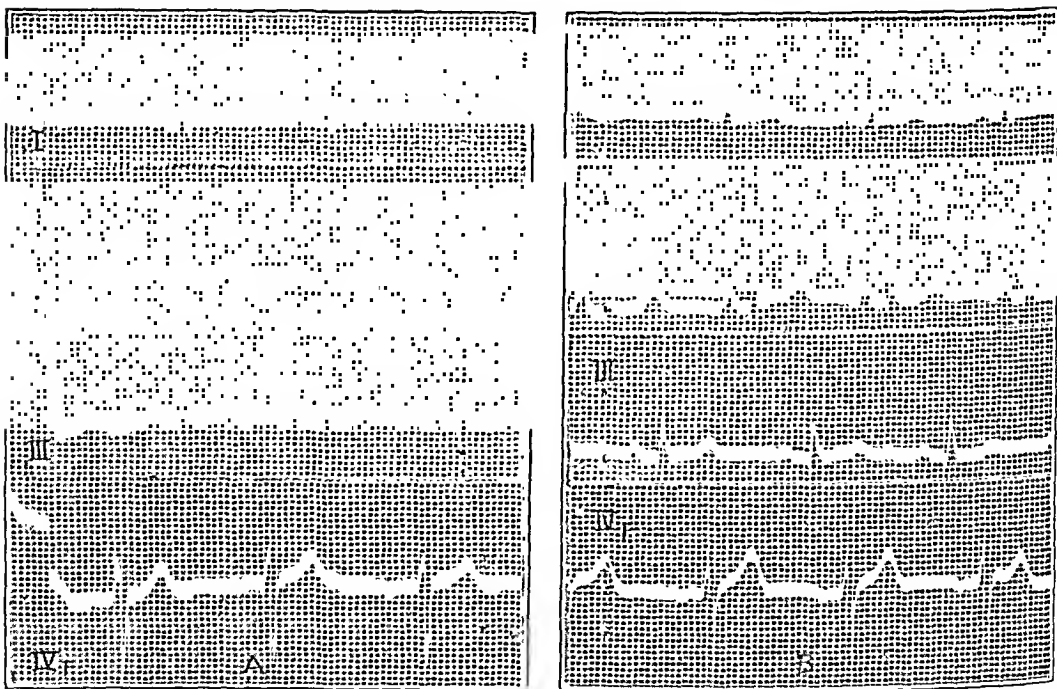


Fig. 13.—Electrocardiograms of J. F. *A*, Sept. 14, 1942, before operation, the rate was 80. The interpretation was normal rhythm with some sinus arrhythmia. The clinical diagnosis was hypertension. The tracing is not entirely normal in contour, but no diagnosis of cardiac pathologic changes can be made from this alone. *B*, Feb. 2, 1943, after operation, the rate was 75. There was sinus rhythm with a low T wave in lead I. The clinical diagnosis was hypertension. Some improvement is indicated when a comparison is made with *A*.

each pair is the last of a series of many tracings. The shortest interval between the operation and the last electrocardiogram is five months, and the longest interval is twenty-two months. In each instance the post-operative electrocardiogram shows improvement when compared with the preoperative tracing.

In the case of J. F. the improvement is minimal, but there was only slight abnormality in the preoperative curve. This is a case of grade 2 arteriosclerotic hypertension, case 8 in this series (fig. 13).

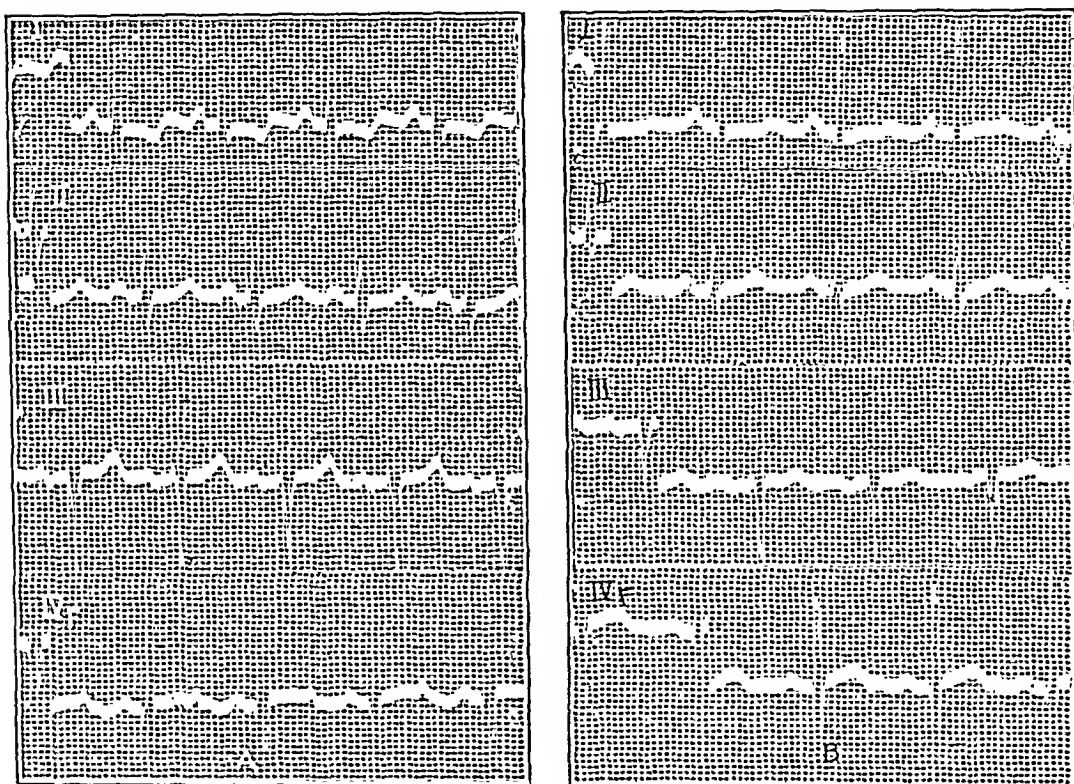


Fig. 14.—Electrocardiograms of L. R. *A*, Jan. 22, 1942, before operation, the rate was 102. The interpretation was sinus tachycardia. The T wave in lead I was inverted, and in lead IV it was diphasic. The ST segment was depressed in lead I. There was pronounced left axis deviation. This is consistent with hypertensive cardiac disease. *B*, Sept. 8, 1942, after operation, there was sinus rhythm. The T wave in lead I was diphasic, and the P wave in lead III was inverted. There was left axis deviation. Definite improvement is noted when a comparison is made with *A*.

In the case of L. R. an electrocardiogram made eight months post-operatively shows that a definitely abnormal and distorted lead I has been restored to a lead that shows only slight depression of the T wave. These tracings belong to a patient with severe vascular occlusion (fig. 14).

Leads I and II in the preoperative curve of J. A. are definitely abnormal, while thirteen months later they are quite normal. This occurred in case 15 (fig. 15).

The preoperative curve of J. T. is a distinctly abnormal curve in all leads except the precordial one. Twenty-two months later this curve is remarkably improved and with the exception of a moderate deformity in lead I is normal. In each case the change took place gradually (case 6, fig. 16).

It should be emphasized that the preoperative curve in each case, except that of J. F., exhibited changes that one might have assumed

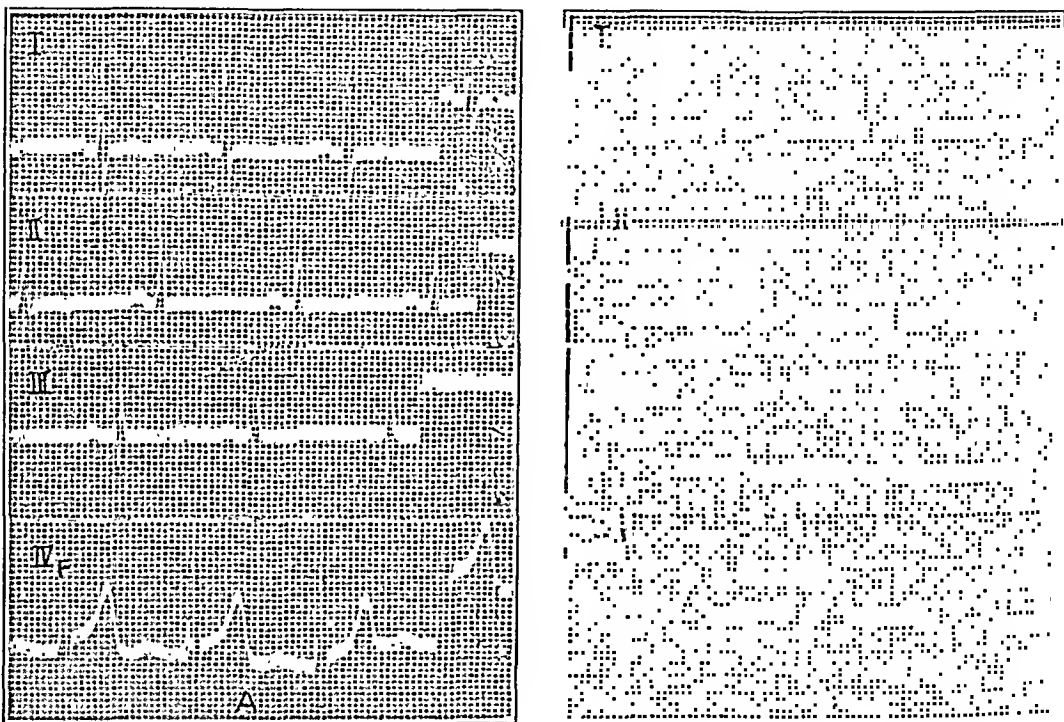


Fig. 15.—Electrocardiograms of J. A. *A*, May 20, 1943, before operation, the rate was 90. There was sinus rhythm. The T wave in leads I and II was inverted, and in lead III it was low. The ST segment was elevated in lead IV. There was evidence of myocardial damage. *B*, June 13, 1944, after operation, the rate was 70. There was sinus rhythm. The T wave in lead III was inverted. There was left axis deviation. Electrocardiographic improvement is noted when a comparison is made with *A*.

were irreversible. In each case, however, alteration began to appear that culminated in a near normal tracing.

*Sensitivity to Epinephrine.*—In our first paper<sup>1</sup> we stated that decrease of sensitivity to epinephrine was noted after splanchnic section. Generally speaking, the hypertensive patient shows an exaggerated response to epinephrine. One to 10 micrograms are injected intra-

venously, preceded by a "sham" injection of isotonic solution of sodium chloride, to test for the emotional or pain response of the patient.

It would be erroneous to believe that the "neurogenic" type of hypertensive patient is especially sensitive to epinephrine; in fact, since such patients already show some continuous vasoconstriction, their response is usually within normal limits. This is also true of animals whose buffer nerves have been removed.<sup>24</sup> Ominous, however, is the finding of a poor or absent response in a patient with a high diastolic pressure. This denotes—just as in the case of the cold pressor test—the con-

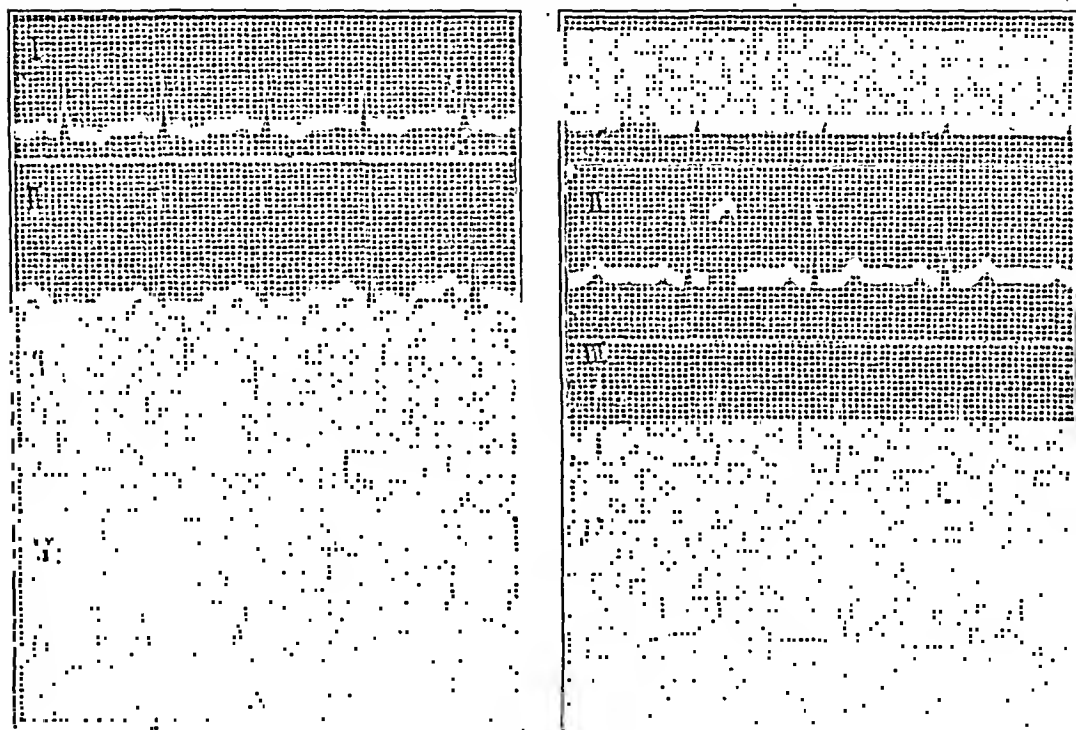


Fig. 16.—Electrocardiograms of J. T. *A*, March 19, 1942, before operation, the rate was 100. The interpretation was sinus tachycardia. The T wave in leads I, II and III was inverted. The clinical diagnosis was hypertension. There was evidence of myocardial damage. *B*, Jan. 11, 1944, after operation, the rate was 80. There was sinus rhythm. The T wave in lead I was depressed. There was moderate right axis deviation and some sinus arrhythmia. The diagnosis was hypertension. Remarkable improvement is noted when a comparison is made with *A*. Except for the moderate deformity in lead I, the curve is within normal limits.

tinuous vasospasm of the premalignant and malignant phase and contra-indicates operation.

24. Thomas, C. B., and McLean, R. L.: Effect of Intravenous Injection of Epinephrine and Angiotonin Before and After Production of Neurogenic Hypertension, *Bull. Johns Hopkins Hosp.* 75:319, 1944.

The diminished response to epinephrine following splanchnic nerve section (fig. 17) is susceptible to different interpretations. It is possible that it measures a decrease of the circulating pressor substance, since the pressor substance sensitizes the blood vessels to epinephrine.<sup>25</sup> It might also mean that the patient after splanchnic section has lost some of his reflex nervous irritability and possibly cannot mobilize his own epinephrine so readily. Certainly patients volunteer the information that much of their "inner nervous tension," much of their emotional palpitation, is gone after operation.

While the test for epinephrine sensitivity throws an interesting sidelight on one of the mechanisms by which splanchnic nerve section acts, it has added little information to the indications for operation and its routine use has not been pursued except in certain cases.

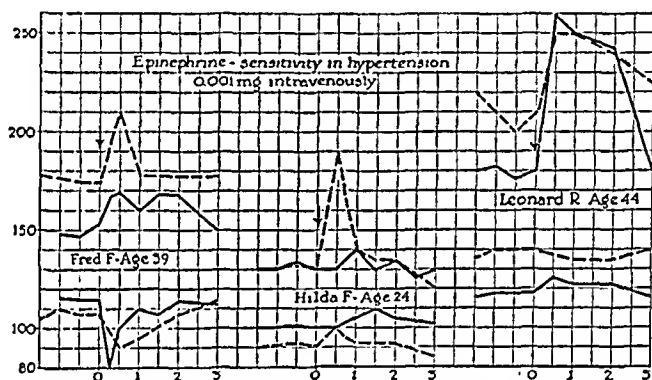


Fig. 17.—Sensitivity to epinephrine before and after splanchnic nerve section. Interrupted lines, period before operation; straight lines, period after operation. In the case of Fred F. the postoperative response was definitely diminished. Note the depressor effect of epinephrine on the diastolic pressure, which is the usual response. In the case of Hilda F. sharp systolic rise, observed before the operation, has been almost entirely eliminated. In the case of Leonard R., the postoperative response is unchanged. This patient belonged to group 3, with hypertension in a premalignant phase. While the patient derived temporary benefit from the operation, his cardiac and renal changes were advanced. He died three years after operation, from a coronary occlusion.

*The Circulation Time.*—When patients are tested with 3 cc. of dehydrochloric acid or with fluorescein administered intravenously, their foot to tongue circulation time varies between twenty and twenty-six seconds in the horizontal position. When the patient is standing still or on a tilting table in the upright position, this is usually lengthened to thirty to forty seconds and one draws a "blank" response more often, i. e., the patient does not experience a sudden bitter taste. After splanchnic nerve section, when the patient is in the erect position, such circu-

25. Heinbecker, P.: Role for Surgeons in Problems of Essential Hypertension, *Ann. Surg.* **112**:1101, 1940.

lation times which are dependent on subjective sensation are so indefinite that their use has been given up. Instead, the fluorescein given intravenously with the aid of an ultraviolet light has given more definite information. The time is greatly prolonged, indicating delayed venous return after splanchnic section, with the patient in the erect position.

*Comment.*—These special studies indicate that much of the vascular strain imposed on organs such as the retina, the heart and possibly the kidney is still reversible if the operation is not delayed too long. This certainly seems to be true of the size of the heart and the electrocardiogram; that the retinal circulation is spectacularly influenced has been reported early by Peet and his co-workers.<sup>26</sup> Most of these beneficial changes can be explained by the reduced tension in the vessels and this in turn by the diminished venous return from the splanchnic area and the lower extremities.

The decrease in sensitivity to epinephrine is an expression of adrenal denervation. Adrenal denervation, as pointed out by Heinbecker,<sup>27</sup> decreases reflex nervous irritability; it also seems, as he pointed out, that the renal pressor substance sensitizes the blood vessels to epinephrine. Clinically, most patients state that an "inner nervous tension" has been relieved, and this statement is being made, without direct questioning, by the illiterate farm hand, by the high tension city dweller or by the pampered only child without an occupation.

We have no evidence to present that the customary renal functional studies show any difference before and after sympathectomy, at least with the patient in the horizontal position; this is the conclusion of Talbot and his co-workers.<sup>14b</sup>

What has impressed us the most is the redistribution of circulation following splanchnic nerve section and its possible influence on the relief obtained. Our blood volume studies carried out with the recent modification of Gregersen<sup>27</sup> are not sufficiently numerous or easy enough to interpret. But the great slowing of circulation time with the patient in the erect position points to the pooling of blood in the denervated areas, with a decrease of venous return. This would account for the disappearance of headaches and dizziness, the disappearance of papilledema, the decrease in spinal fluid pressure, the decrease in the size of the heart, the improvement in the electrocardiogram and the disappearance of palpitation, all of which may occur without a notable drop

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26. Peet, M. M.; Woods, W. W., and Braden, S.: The Surgical Treatment for Hypertension: Results in 350 Consecutive Cases Treated by Bilateral Suprardiaphragmatic Splanchnicectomy and Lower Dorsal Sympathetic Ganglionectomy, *J. A. M. A.* **115**:1875 (Nov. 30) 1940.

27. Gregersen, M. I.: A Practical Method for the Determination of Blood Volume with the Dye T-1824, *J. Lab. & Clin. Med.* **29**:1266, 1944.

in blood pressure, which have been interpreted by Volini and Flaxman<sup>28</sup> as being entirely nonspecific and which could result after any operation.

It is well to regard splanchnic nerve section and dorsolumbar sympathectomy as having a vast influence on the blood depots of the splanchnic area and on those of the lower extremity. It is sufficiently known that the spleen, liver, kidney and gastrointestinal tract may hold a considerable amount of blood, and so does the subpapillary venous plexus of the skin.<sup>29</sup> When the patient is in the erect position, the sympathetic nervous system is the one that empties such depots.

When we deprive the hypertensive patient of his vasomotor mechanism, his adjustment to the erect posture will suffer. Starr's studies on the incoordination of circulation as determined by the response to arising<sup>30</sup> indicate that when the vasomotor apparatus is insufficient the cardiac output increases and should this second mechanism fail involuntary muscle spasms occur before collapse.

In examining patients shortly—up to four to six weeks—after bilateral splanchnic nerve section and dorsolumbar sympathectomy, they show the postural hypotension<sup>2</sup> and the postural dyspnea<sup>31</sup> which is characteristic of a successful denervation. However, this is compensated within a few weeks, and the postural tachycardia, which is present from the first, remains the longest. This increase in cardiac output is tolerated well by the properly selected patient, but attention should be called to patients (case 6) who show signs of coronary insufficiency for a long time. One of us (G. de T.) observed a patient who had a transdiaphragmatic sympathectomy done elsewhere and who not only had slight reduction of blood pressure but could hardly sit up or walk without becoming dyspneic; yet he had no evidence of congestive heart failure or an attack of coronary thrombosis. The surgeon must be aware, then, of the fact that splanchnic nerve section is going to throw an additional burden on the heart of the patient in the erect position and that the preoperative study of the myocardial reserve is important.

Since most blood depots can be emptied by carbon dioxide, the study of the pressor response to carbon dioxide seems a fruitful and simple method of study. Such studies are now in progress with the patients in the horizontal and erect positions, before and after operation.

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28. Volini, I. F., and Flaxman, N.: Effect of Nonspecific Operations on Essential Hypertension, *J. A. M. A.* **112**:2126 (May 27) 1939.

29. Wollheim, F.: Die Blutreservoirs des Menschen, *Klin. Wchnschr.* **12**: 12, 1933.

30. Starr, J.: Clinical Studies on the Incoordination of Circulation as Determined by the Response to Arising, *J. Clin. Investigation* **22**:813, 1943.

31. Bordley, J.; Goldstone, M., and Dandy, W. E.: The Treatment of Essential Hypertension by Sympathectomy, *Bull. Johns Hopkins Hosp.* **72**:127, 1943.

*The Rate of Recurrence After Operation.*—No report on the surgical treatment of cancer would fail to contain statistics on the percentage of recurrence after certain periods. We have studied our material from this aspect. Recurrence was defined as return of the diastolic pressure to the preoperative level. This may seem to be an arbitrary and rather lax definition, but it must be remembered that even when preoperative levels are reached the dynamics of circulation have been changed and that the life of the patient may be prolonged by diminished stress on some of the supradiaphragmatic structures.

Table 12 shows the number of recurrences among 41 patients of groups 1 and 2, since all patients belonging to the third group died within a year. Of the 8 patients with recurrence 2 belonged to the first group and both needed reoperation, after which their pressures fell. Of the second group, the 6 patients whose diastolic pressures rose to the preoperative level were carefully scrutinized. It is primarily due to these recurrences that we refuse to operate on patients who either have a

TABLE 12.—*Recurrence of Hypertension After Splanchnic Nerve Section in Fifty-One Cases Observed from 1940-1943*

| Group | Total Number | Number of Recurrences * | Probable Causes   |
|-------|--------------|-------------------------|---|
| 1     | 17           | 2                       | Both patients had incomplete operations; pressure fell after reoperations |
| 2     | 24           | 6                       | Atheromatosis of large vessels or early malignant phase                   |
| 3     | 10           | All died                |   |

\* Recurrence: rise of diastolic pressure to preoperative level.

striking enlargement and rigidity of the aorta or exhibit the continuous vasospasm of severe benign nephrosclerosis or pyelonephritis, which we regard as the premalignant phase.

This table is a strong argument for operating on the patients in the first group, since with the exception of 2 patients who had technically incomplete operations all showed improvement or complete return to normal. The group of 17 patients will have to be followed for the next ten to twenty years for the final appraisal of the value of sympathectomy to hypertensive patients.

#### GENERAL COMMENT

Since detailed comments were made under the various headings, we simply wish to reemphasize here our present attitude toward this operation. If surgeons are really going to face this issue squarely, they must urge an early operation on all patients with group 1 hypertension whose diastolic pressures exceed 90 mm. of mercury. These patients are overwhelmingly asymptomatic and are recognized at preemployment, prein-



duction or insurance examinations. A distinction should be made between the hypertension of these patients and the hypertension of adolescents, who may come from hypertensive families and who during their period of growth and possibly increased pluriglandular function show a higher than normal pressure which may become normal in early adult life. We are watching such a boy of 15 and may have to operate on him if his pressure does not come back to normal. Lawrence<sup>32</sup> found 9.5 per cent of 220 students to show abnormally elevated pressures and gained the impression that most of them came from hypertensive families, that their cold pressor response was frequently abnormal and that they were in a prehypertensive stage. For this group we advise frequent reexaminations, at three month intervals. No type of medical treatment seems effective to prevent the full-blown appearance of juvenile hypertension.

Another group of patients who should be strictly separated from early juvenile hypertensive patients are those with transient nervous hypertension. Rogers and Palmer<sup>33</sup> found in examining 1,574 applicants studied at the Office of Naval Procurement in Boston that 14 per cent of them showed a short, transient hypertension with a normal cold pressor response. They felt that their prognosis is excellent, and in just how many of them persistent hypertension will develop is unknown.

We postulate, then, a persistent casual hypertension<sup>34</sup> of over 140 systolic and 90 diastolic in persons between 18 and 25 before we consider them for operation. By a casual blood pressure, we mean that it is recorded during the course of normal activity, during the day. That their basal blood pressure after bed rest, during sleep or under the influence of sedatives goes down to normal and puts them in the first group should not lull the physician into a false sense of security. It is in this group with no or minimal organic changes that our best results are obtained.

The experienced internist knows that the prognosis of these juvenile hypertensive patients is unfavorable. While the rate of progress is unpredictable, the middle-aged hypertensive patient will begin to show enough symptoms and organic damage so that he is more apt to be referred for operation. He can derive benefit if he fulfils our requirements for the second group, but some organic damage must remain. Whether his life has been prolonged is a matter for long term statistics to show. The subjective improvement, which in our opinion is due to a

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32. Lawrence, H. E.: The Blood-Pressure of Adolescents, *New England J. Med.* **228**:381, 1943.

33. Rogers, W. F., and Palmer, R. S.: Transient Nervous Hypertension as a Military Risk, *New England J. Med.* **230**:39, 1944.

34. Alam, G., and Smirk, F. M.: Casual and Basal Blood-Pressures: I. In British and Egyptian Men, *Brit. Heart J.* **5**:152, 1943.

redistribution of the circulating blood volume and which has lasted in our material for three to five years, is in itself an important consideration and takes the place of small repeated venisections. In fact, if a small venisection does not bring about subjective improvement or a fall in blood pressure, splanchnic nerve section may prove to be useless.

The surgeon need not consider the patients in the premalignant or malignant phase, since there is no benefit to be derived from a surgical procedure. The argument is frequently brought forward that all other types of treatment have failed and that the patient has nothing to lose since his prognosis is so poor. We feel that it is useless and unfair to put a patient through a large, two stage operation, since we have never seen any benefit at this stage. Occasional spectacular results as reported in the literature may be due to nephritic exacerbation and remission of chronic benign nephrosclerosis, and patients with such results should not be classified as belonging to the group of patients with malignant hypertension.

Another conclusion which our observations justify is rather startling. Considerable effort has been spent by investigators to separate the "neurogenic" from the renal type of hypertension. Page and his group advanced the use of high spinal anesthesia and felt that the "neurogenic" group shows a considerable fall in blood pressure as contrasted with the renal group.<sup>11</sup> This has certainly not been our experience; in operating on a large number of older arteriosclerotic patients with hypertension under spinal anesthesia, we have repeatedly observed a severe fall in blood pressure; yet they could hardly be regarded as suitable for sympathectomy. Grimson and his co-workers produced neurogenic hypertension in dogs and found that nothing short of a total sympathectomy would abolish such hypertension.<sup>12</sup> For this reason they reject splanchnic nerve section as being only a partial sympathectomy; when their method is used the compensatory tachycardia which develops in the erect posture is inhibited, and this in our opinion produces an even greater incoordination of circulation than splanchnic section, since it deprives the patient from increasing his cardiac output.

In our material it is the renal group which has shown the best clinical results from splanchnic nerve section. As pointed out elsewhere,<sup>35</sup> patients with pyelonephritis, post-toxic hypertension, streptococcal nephritis and rheumatic renovascular damage are favorable candidates provided the vascular lesion is not too far advanced. On the other hand, the "neurogenic" group has not done well. The fluctuations of their pressures have not been abolished, and their emotional "hypothalamic"

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35. de Takats, G., and Fowler, E. F.: The Surgical Treatment of Hypertension: III. Neurogenic Versus Renal Hypertension from the Standpoint of Operability, to be published.

outbursts are not eliminated and continue to operate on the vascular system. The explanation for this phenomenon is far from being clear. It may be, as Grimson feels, that more of the sympathetic nervous system has to be removed in this group of patients.<sup>12</sup> However, a few of our total sympathectomies which were done in several stages have not shown any improvement over the transdiaphragmatic approach. We are more impressed with the possibility that the "neurogenic" hypertension may operate through a pluriglandular mechanism and is not mediated by the splanchnic nerves at all.

It is well established that the posterior lobe of the pituitary is readily activated by nervous stimulation and that indeed it completely atrophies if the pituitary stalk is sectioned.<sup>36</sup> It also seems established that when the stalk is sectioned in man, as occurred in Dandy's case,<sup>37</sup> a low blood pressure develops in addition to the diabetes insipidus. To round out the argument, the clinical studies of Griffith<sup>38</sup> should be cited, who found in a certain small percentage of hypertensive patients that their serum contains an excess of the antidiuretic hormone. The test is simple; only 1 cc. of the patient's serum is needed; this is injected intraperitoneally into rats, and their water-retaining ability is studied. In hypertensive patients with positive tests for the antidiuretic hormone of the pituitary, Prendergrass, Hodes and Griffith<sup>39</sup> advocated radiation of the pituitary gland. A total dose of approximately 1,000 r must be delivered, and the reaction to the test for the antidiuretic hormone must become negative. They also stated that if the response to the radiation fails in regard to blood pressure and to the test the majority of such patients have positive tests for gonadotropic hormones and should be treated by diethyl stilbestrol or testosterone respectively. In such patients hypersecretion from the posterior lobe is secondary to hypersecretion from the anterior lobe.

We are unable to verify or disprove this contention at present, but the point of a pluriglandular type of hypertension, governed by the pituitary and activated by a nervous mechanism, has much in its favor.

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36. Fulton, J. F.: *The Physiology of the Nervous System*, ed. 2, London, Oxford University Press, 1943.

37. Dandy, W. E.: Section of the Human Hypophysial Stalk: Its Relation to Diabetes Insipidus and Hypophysial Function, *J. A. M. A.* **114**:312 (Jan. 27) 1940.

38. Griffith, J. Q., Jr.; Corbet, H. O.; Roberts, E., and Lindauer, M. A.: Studies of Criteria for Classification of Arterial Hypertension: V. Types of Hypertension Associated with the Presence of Posterior Pituitary Substance, *Am. Heart J.* **21**:77, 1941.

39. Prendergrass, E. R.; Hodes, P. J., and Griffith, J. Q., Jr.: Irradiation of the Pituitary Gland in Posterior Lobe Hyperfunction Controlled by Biologic Tests, *Am. J. Roentgenol.* **46**:673, 1941.

Such patients will not respond to splanchnic nerve section, and a simple clearcut biologic test would be most welcome to separate them from the operable patients.

#### SUMMARY

The surgical treatment of hypertension, based on the preoperative and postoperative study of 52 patients, is discussed in detail. For an improvement in results a rigid selection of cases is advocated. A group representing a clearcut indication is separated from one in which the indication is relative and is debatable. A third group, consisting of the patients with premalignant and malignant hypertension, is not regarded as being suitable for operation. The criteria for establishing the group with premalignant hypertension are defined. Some of the problems of anesthesia, especially the avoidance of accumulation of carbon dioxide, are discussed. The surgical procedure is described step by step, with illustrations. The transdiaphragmatic approach, to which a unilateral renal biopsy is added, has been employed in this series. The follow-up system is described, on the basis of which the results are tabulated in the three groups. In the 17 patients in group 1, the response was most gratifying. Only 2 had recurrent hypertension, which was corrected after completion of a technically incomplete operation. Six patients showed recurrence in the second group; these were analyzed and reasons found for the organic, irreversible lesions, which can be detected preoperatively. No results were obtained in the third group of patients.

The value of renal biopsies was discussed and also the help that special postoperative studies relating to eyegrounds, roentgenograms of the chest taken at a distance of 2 meters, electrocardiograms, epinephrine sensitivity and circulation times offer. The redistribution of circulation through the effect of splanchnic nerve section on blood depots has been stressed. This field offers vast opportunities for future study. So far no single or combined method of treatment can be recognized which would give rigidly selected patients with hypertension as much benefit as the transdiaphragmatic splanchnic nerve section combined with dorsolumbar sympathetic ganglionectomy.

## FRACTURES OF THE CARPAL SCAPHOID BONE

An Analysis of Sixty-Six Cases

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THE CORRECT treatment of fractures of the carpal scaphoid bone which are diagnosed early is adequate prolonged fixation. This treatment has long been recognized, but in spite of this realization a large percentage of fractures go undiagnosed and therefore untreated. This delay in diagnosis is conducive to nonunion and arthritic changes, which increase the difficulty of treatment and make results ungratifying. Mildness of symptomatology often causes procrastination of the patient in seeking medical advice. The relative infrequency of fractures of the carpal scaphoid bone in civil life makes it difficult to collect and evaluate sufficient cases to arrive at the type of treatment needed for these fractures, particularly cases in which there has been considerable delay in seeking attention.

In the armed forces, with careful medical supervision of a large group of young adults, an increasing number of fractures of the carpal scaphoid bone have been diagnosed. The series of 66 cases reported in this paper was seen over a period of two years at Harmon General Hospital and LaGarde General Hospital, constituting 5 per cent of all fractures seen during this time.

The exacting and prolonged physical demands of military training are such that fractures of the carpal scaphoid bone produce pronounced disability and result in prolonged morbidity. Military service also brings to light old undiagnosed fractures with nonunion which were incurred prior to the patients' entrance into service. In this study 8 cases of this type were seen, but they have not been included in the series.

In spite of the wide availability of x-ray facilities and the knowledge of these factors, early diagnosis is not the rule. This is immediately apparent in the table.

### FACTORS IN DIAGNOSIS

In this series 42 per cent of the fractures of the carpal scaphoid bone were not diagnosed at the time of injury. Five patients, or 7 per cent, failed to report the injury for several weeks after its incurrence. In 35 per cent of this series either the fractures were diagnosed as sprains and not examined roentgenologically or the roentgenograms

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From the Orthopedic Section, Harmon General Hospital, Longview, Texas.

were reported negative for fracture and the diagnosis missed. Because of these missed diagnoses, the convalescence was unduly prolonged and invaluable weeks and months of time lost to the soldier.

*Healing Time for Fractures of the Scaphoid Bone*

| Elapsed Time<br>Until Diagnosis,<br>Days | No. of<br>Cases | Roentgenograms at Time of Injury |          |      | Duration of<br>Treatment,<br>Mo. | Nonunion' |
|--|-----------------|----------------------------------|----------|------|----------------------------------|-----------|
|  |                 | Positive                         | Negative | None |                                  |           |
| 1-30                                     | 38              | 36                               | 2        | 0    | 3.7                              | 0         |
| 30-60                                    | 5               | 0                                | 2        | 3    | 4.3                              | 0         |
| 60-120                                   | 5               | 0                                | 1        | 4    | 5.1                              | 0         |
| 120-180                                  | 6               | ..                               | 2        | 4    | 5.5                              | 0         |
| Over 180                                 | 12              | ..                               | 3        | 9    | 7.5                              | 10        |
| Totals.....                              | 66              | 36                               | 10       | 20   |                                  | 10        |

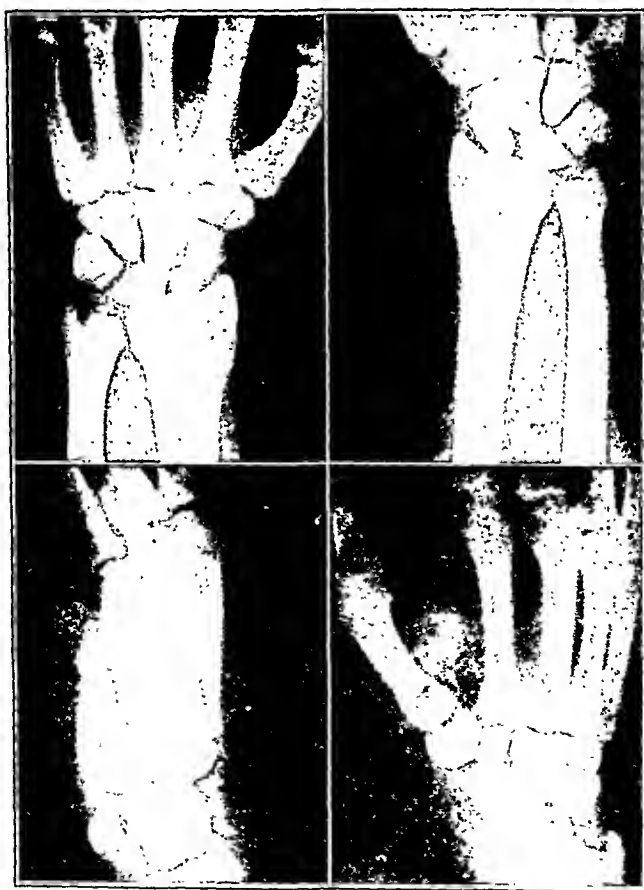


Fig. 1.—Fresh fracture of the carpal scaphoid bone. Note that the fracture is seen in only one oblique view.

Such a large number of missed diagnoses shows that one must be on the alert for fractures of the carpal scaphoid bone to make an early diagnosis. In cases in which pain and swelling of the wrist persist,

and especially when the pain and tenderness are in the region of the anatomic snuffbox, careful reevaluation and reexamination of the wrist are indicated.

Because of the large number of negative roentgenograms, it is our belief that all cases of injury to the wrist should have, in addition to the routine anteroposterior and lateral views, semilateral roentgenograms at approximately 30 and 60 degree angles. With the foregoing procedure, in only 2 cases were fractures of the carpal scaphoid bone not diag-

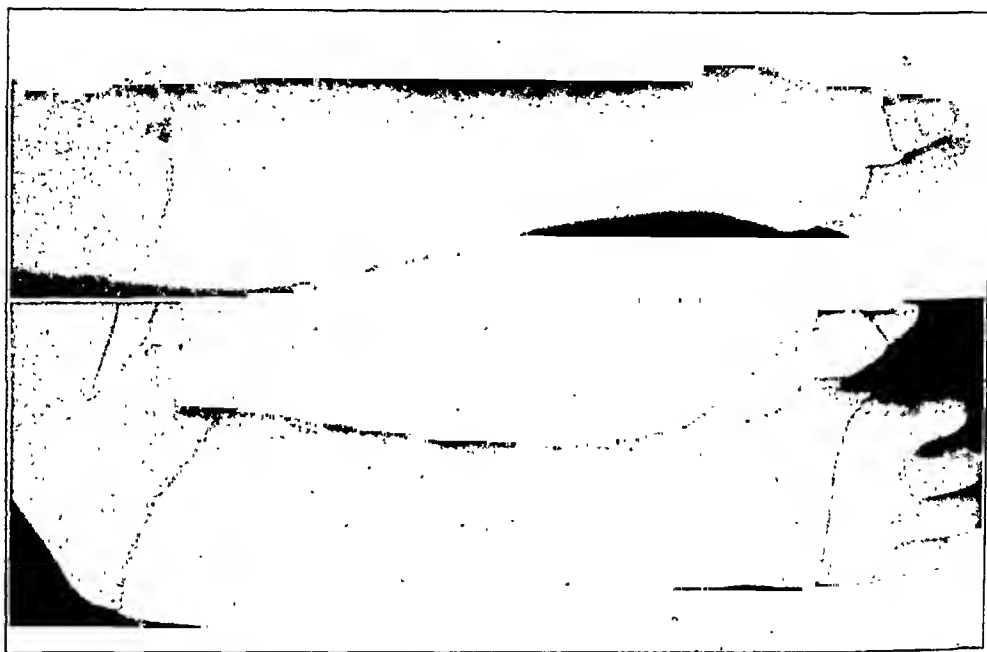


Fig. 2.—Cast for immobilization, incorporating thumb to distal end of proximal phalanx.

nosed at the time seen, and in these 2 diagnoses were made on reexamination, three weeks later (fig. 1).

#### SYMPTOMS

The clinical picture is well known and has been adequately discussed by Soto-Hall and Haldeman.<sup>1</sup> In older fractures the persistent pain in the anatomic snuffbox is a constant finding, with weakness and pain after exertion. Swelling and moderate limitation of motion are less constant, but the presence of any of these conditions is sufficient to warrant detailed examination of the wrist.

1. Soto-Hall, R., and Haldeman, K. O.: The Treatment of Fractures of the Carpal Scaphoid, *J. Bone & Joint Surg.* **16**:822-828, 1934.

## TREATMENT

Complete and prolonged immobilization is the accepted treatment in all cases. Even ten months after injury fractures which have not been treated warrant a trial of immobilization, as 15 per cent or more will give satisfactory results from this treatment alone.

Reduction of fractures of the carpal scaphoid bone is seldom necessary. When seen in association with dislocation of the semilunar bone, the fragments of the carpal scaphoid bone are usually in good position after the semilunar bone has been reduced. In this series, there are 2 cases of this type.

Immobilization by a skin-tight cast involving the thumb and extending from the elbow to the distal palmar crease was the method used. The wrist was held in moderate dorsiflexion and slight radial deviation.

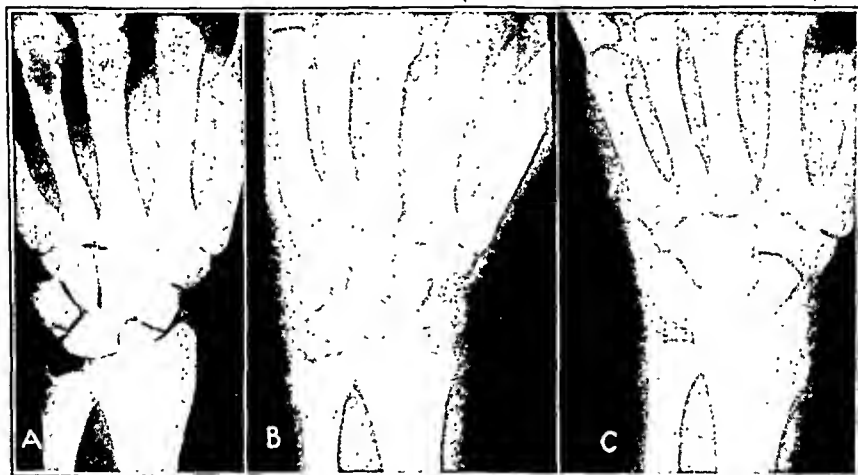


Fig. 3.—Delayed union of the carpal scaphoid bone. *A*, original picture, four months after injury. *B*, three months later, showing beginning of union and aseptic necrosis of proximal fragment. *C*, after six months of treatment. Complete union is present. Revascularization is practically complete.

The thumb, held in abduction and extension, was included to the distal phalanx (fig. 2).

Casts were changed when they became loose due to atrophy of the forearm muscles. This atrophy is minimized by use of the fingers during immobilization. Check roentgenograms in all positions were taken every six weeks and immobilization continued until the fracture line completely disappeared. Inclusion of the thumb is essential for two reasons. First, the fragments are thus held in most intimate contact. Second, complete immobilization cannot be accomplished unless this is done. Union rarely occurs when the thumb is not included.



## COMMENT

In 56 cases, or 85 per cent of the series, the fracture healed, without arthritic changes, by prolonged immobilization. In the oldest to heal, it had been nine months from the time of injury to instigation of immobilization. This treatment appears worthy of trial in all fractures under ten months old. In our series all fractures under six months healed satisfactorily. The presence of osteoporosis of the carpal scaphoid bone due to trauma (Preiser's disease) was no bar to healing in the 6 cases seen. Immobilization was continued until complete revascularization occurred. This was evidenced by gradual decrease of sclerosis of the fragment and restoration of uniform density as seen by the roentgenogram (fig. 3).

Operative intervention was not instituted until after at least two months of immobilization the fracture failed to show improvement. Operative treatment was performed in 10 cases. Six fractures healed with good results. In 2 cases of fracture showing pronounced arthritic changes the distal fragment was removed, with 50 per cent good results.

After immobilization in both operative and nonoperative cases, recovery of function was surprisingly rapid. All patients regained full motion and strength after only one month of use and physical therapy. This was in a great part due to the continuous use of the fingers by physical and occupational therapy during the immobilization period, in spite of the fact that these fractures were immobilized six to eight months.

## CONCLUSIONS

1. In 85 per cent, or 56, of a series of 66 cases fractures of the carpal scaphoid bone seen within twelve months after injury healed by prolonged immobilization in a skin-tight cast, including the thumb. All fractures less than six months old healed by this method.

2. Diagnosis at time of injury is possible in most cases provided the surgeon is aware of the fracture and makes multiple views of the wrist at the time of injury, repeating these views if symptoms persist and when checking union. These views are discussed in detail.

# PERICORONARY NEURECTOMY IN ABOLISHING ANGINAL PAIN IN CORONARY DISEASE

An Experimental Evaluation

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A SURGICAL procedure to be of optimum value in the treatment of coronary disease must simultaneously improve the coronary circulation, block vasomotor reactions and eradicate anginal pains.<sup>1</sup> Operations now in use cannot achieve full benefit for the patient with coronary disease, as their specific objective is limited either to the interruption of nerve pathways that may carry pain impulses or to the improvement of the coronary circulation.

Cervical or dorsal sympathectomy may interrupt some impulses originating from the coronary vessels or the myocardium; yet it is not satisfactorily demonstrated experimentally that all important pathways carrying impulses to and from the coronary arteries are cut or that an improvement in coronary circulation follows. Cutler<sup>2</sup> stated, "My own experience in this field comprises a considerable number of surgical attacks on the sympathetic apparatus in the neck and on the upper two dorsal ganglia. I have never been convinced that the relief afforded by such a procedure was complete or lasting." More recently, Willius<sup>3</sup> wrote that "cervical sympathectomy and its various modifications as well as paravertebral injections of procaine hydrochloride and absolute

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From the Laboratory of Surgical Research, Harvard Medical School and the Surgical Service of the Peter Bent Brigham Hospital.

1. (a) Fauteux, M.: Positions actuelles du traitement chirurgical de l'angine de poitrine, *Union méd. du Canada* 69:829, 1940; (b) Études expérimentales sur le traitement chirurgical des coronarites, *ibid.* 72:1260, 1943; (c) La neurectomie péricoronarienne associée à la ligature de la grande veine coronaire dans le traitement de certaines formes de la maladie coronarienne, *ibid.* 74:424, 1945; (d) Treatment of Coronary Disease with Angina by Pericoronary Neurectomy Combined with Ligation of the Great Cardiac Vein, *Am. Heart J.* 31:260, 1946.

2. Cutler, E. C.: The Surgical Treatment of Pain, *New England J. Med.* 218:422, 1938.

3. Willius, F. A.: Coronary Disease: Certain Significant Contributions Made During the Last Quarter Century, *Minnesota Med.* 26:33, 1943.

alcohol . . . have gradually but hopefully lost their appeal." On the other hand, methods proposed to revascularize the heart, which, according to their advocates, increase efficiently the blood supply to myocardial tissues, are not designed to eliminate reflexes originating from diseased coronary arteries which can lead to vascular spasms, pain and primary ventricular fibrillation.

For these reasons, it appeared to one of us (M. F.) some years ago that it would be highly advantageous to devise an operation which would simultaneously accelerate the development in size of the natural coronary anastomosis and block the reflexes concerned with coronary vasomotor disturbances, such as primary ventricular fibrillation and sudden death. Such a procedure should also eradicate anginal pains.

Since it was known through experimental and clinical evidence of other investigators that venous ligation does aid in opening and dilating the arterial anastomosis of the extremities to the extent that gangrene can be avoided in many instances of arterial occlusion, it was thought that coronary venous ligation could help substantially to realize the first objective. Experimental<sup>4</sup> and clinical<sup>5</sup> evidence seems to support this view. It was also assumed that the procedure described by one of us (M. F.) under the name of pericoronary neurectomy could be of great value in achievement of the second objective.

Extensive experimental studies were carried out by one of us (M. F.). The results obtained show unquestionably the respective value of the two procedures as well as their respective limitations. It may be of interest to summarize briefly certain facts concerning the results acquired in these experiments.<sup>6</sup> In one group of dogs, used as a control series, the circumflex artery was ligated at its origin. Twenty per cent of the animals survived. In a second group, prepared in advance by coronary venous ligation alone, the circumflex artery was ligated as in group 1. Fifty per cent of the dogs survived. It is interesting to note that most of the animals lost died soon after the arterial occlusion, apparently due to primary ventricular fibrillation. In a third group, prepared in advance by pericoronary neurectomy alone, ligation of the circumflex artery was done as in the previous group. Sixty per cent of the animals lived. Another interesting point to note is that most of the dogs that died suc-

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4. (a) Gross, L.; Blum, L., and Silverman, G.: Experimental Attempts to Increase the Blood Supply to the Dog's Heart by Means of Coronary Sinus Occlusion, *J. Exper. Med.* **65**:91, 1937. (b) Fauteux, M.: Experimental Study of the Surgical Treatment of Coronary Disease, *Surg., Gynec. & Obst.* **71**:151, 1940.

5. Fauteux, M., and Palmer, J. H.: Treatment of Angina Pectoris of Atheromatous Origin by Ligation of the Great Cardiac Vein, *Canad. M. A. J.* **45**:295, 1941.

6. These experimental studies are to be reported in detail and discussed in a monograph which is in preparation.

cumbed much later than those of the group with venous ligations. Apparently they died of cardiac failure due to cardiac ischemia. In a fourth group, prepared in advance by pericoronary neurectomy and coronary



Fig. 1.—Section of a nerve resected from the heart of a dog during pericoronary neurectomy.

venous ligation, the circumflex artery was again tied, as in the other groups. The survival rate rose to 86 per cent.

The following conclusions were reached regarding these two procedures. Coronary venous ligation helps to open and dilate the coronary

anastomotic branches and consequently encourages collateral circulation. The postoperative course in a series of patients who had ligation of the great cardiac vein alone shows the beneficial effect of this operation. All these patients, who were unable to work before operation, have returned to work. In 3 cases five years have elapsed since the ligation of the great cardiac vein, and in 4 cases four years have elapsed since operation. The fact that the patency of the newly opened coronary anastomosis is not only an immediate and temporary effect has been demonstrated elsewhere.<sup>1d</sup> Yet it is obvious that this procedure does not prevent the initiation of reflexes and, therefore, does not seem to diminish the incidence of primary ventricular fibrillation. This is in accordance with the results obtained by other investigators.<sup>7</sup> It does not mean, however, that coronary venous ligation has no therapeutic value. Applied to the heart, the beneficial action of venous occlusion is often masked by deleterious reflexes which rapidly follow after sudden coronary occlusion. When the reflexes are blocked, the value of this measure appears more clearly. This is shown by the results obtained in the fourth group and in the group of Beck and Mako, in which ligation of the great cardiac vein was combined with a partial arterial occlusion, which to a certain extent prevents deleterious reflexes.

That pericoronary neurectomy definitely aids in prevention of primary ventricular fibrillation and rapid death after coronary ligation is well demonstrated by the results obtained in group III. It apparently also helps to improve collateral circulatory conditions by abolishing reflexes interfering with the coronary anastomotic system. Alone, however, it does not suffice to prevent cardiac ischemia or secondary death in every instance. When the two procedures are combined at the same operation, the importance and value of their association appear clearly.

One important point that remained unsolved by these experiments is to what extent this type of operation could diminish the incidence of pain in coronary disease. This question is studied in the present report.

The experimental method for studying cardiac pain responses, although not beyond criticism, has been fairly well standardized. It was described and used by Sutton and Lueth.<sup>8</sup> The procedure is as follows: With the animal under ether anesthesia, without the use of morphine or other sedative and with artificial respiration, the chest was opened in the fifth left intercostal space, the parietal peri-

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7. Beck, C. S.: Natural and Artificial Collateral Circulation in the Heart, in *Blood, Heart, and Circulation: A Symposium*, American Association for the Advancement of Science, Washington, D. C., 1940, p. 133. Beck, C. S., and Mako, A. E.: Venous Stasis in the Coronary Circulation: An Experimental Study, *Am. Heart J.* **21**:767, 1941. Gross, Blum and Silverman.<sup>4a</sup>

8. Sutton, D. C., and Lueth, H. C.: Pain: Experimental Production of Pain on Excitation of the Heart and Great Vessels, *Arch. Int. Med.* **45**:827 (June) 1930.

cardium being exposed. Through a small incision in the parietal pericardium, a ligature was passed around the ramus descendens of the left coronary artery, without being tied. This ligature was passed through a flanged glass tube, which led the ligature to the surface. A purse string suture closed the pericardial incision and at the same time included the flange of the glass tube, thus fixing the tube in place. The proximal end of the tube was sutured in the wall of the chest, and the incision was closed, care being taken to remove any pneumothorax. After three or four hours, when the animal had completely recovered from the anesthesia, was active and showed little shock from the operation and apparently no pain, the cardiac pain test was carried out. By fixation of the external portion of the glass tube and traction on the ligature, the artery can be temporarily occluded. The signs demonstrating pain in the dog, according to Sutton and Lueth, were restlessness, rigidity of the left foreleg, changes in the amplitude and rate of the respirations, nausea, salivation, vomiting and whining. Katz, Mayne and Weinstein<sup>9</sup> and White, Garrey and Atkins,<sup>10</sup> who carried out similar tests in dogs, described identical signs. Sutton and Lueth considered that the pain response is due solely to the interference with the coronary blood flow and not to any adventitious factors incidental to the procedure itself. Katz, Mayne and Weinstein expressed the opinion that the positive response is due to compression of afferent fibers enclosed within the sheaths of the coronary vessels and not to occlusion of the coronary artery by the ligature and the consequent change in the flow of the blood. This test has been considered accurate enough to be used as a means of evaluating the effectiveness of various surgical procedures to interrupt the sensory pathways of the heart.<sup>11</sup>

#### EXPERIMENTAL STUDIES

In the present investigation, the procedure used was similar to that described by Sutton and Lueth. The pain reaction was studied in 20 dogs, divided into two groups of 10 animals each.

*Group I (Control Group).*—The animals were anesthetized with intratracheal ether under positive pressure. The heart was exposed through a

9. Katz, L. N.; Mayne, W., and Weinstein, W.: Cardiac Pain: Presence of Pain Fibers in the Nerve Plexus Surrounding the Coronary Vessels, *Arch. Int. Med.* **55**:760 (May) 1935.

10. White, J. C.; Garrey, W. E., and Atkins, J. A.: Cardiac Innervation, *Arch. Surg.* **26**:765 (May) 1933.

11. White, J. C.: Experimental and Clinical Studies in the Surgical Treatment of Angina Pectoris, *Ann. Int. Med.* **7**:229 (Aug.) 1933. Cutler, E. C., and Shambagh, P.: Total Thyroidectomy in Angina Pectoris, *Am. Heart J.* **10**:221, 1934. Moore, R. M., and Singleton, A. O.: Peripheral Course of Pain-fibers Supplying Coronary Arteries and the Myocardium, *Proc. Soc. Exper. Biol. & Med.* **32**:1492, 1935. White, Garrey and Atkins.<sup>10</sup>

partial resection of the third and fourth left ribs. The pericardial sac was opened, and the ramus descendens of the left coronary artery was exposed. The vessel was isolated from the myocardial tissue sufficiently to pass a ligature around it. This ligature was led through the thoracic cavity to the surface by use of a small straight cannula. The cannula was sutured tightly into the wound so that pneumothorax was not a postoperative complication. After this procedure the dogs were allowed to regain consciousness, and when fully alert, three to four hours after operation, they were ready for observation of responses to sudden occlusion of the coronary vessel. Electrocardiograms were recorded after the operation and during the pain tests. It should be emphasized that in no case was the animal allowed to suffer unnecessarily.

PROTOCOL 1 (dog 195-43).—Three and one-half hours postoperatively, the dog was active and seemed fairly normal. Traction was applied to the ligature for fifteen seconds. This caused the dog to shift about, and toward the end the left leg was lifted. Respirations became definitely depressed. The mild restlessness disappeared as soon as the traction was released. After a rest period, an occlusion of eighteen seconds produced definite depression in the respiratory excursion. At the end of eighteen seconds, the ligature severed the artery. No changes were noted for ten to fifteen seconds. After this there were violent whining and stiffening of the legs, particularly the front legs. At autopsy, it was found that the ramus descendens had been divided 1.5 cm. from its origin.

PROTOCOL 2 (dog 230-43).—Four hours after operation, the dog was up and around the cage and was fairly active. Occlusion lasting fifteen seconds produced repeated lifting of the left foreleg and respiratory depression. After a rest period, occlusion of the artery for twenty seconds resulted in a repetition of the symptoms described and, in addition, the left foreleg was held in a cramped flexed position. A rest period was allowed, and the next occlusion lasted one minute. The animal repeatedly tried to move away. There was no movement of either leg. A rest period followed. The fourth occlusion lasted two minutes. About five seconds after the beginning, the left foreleg was lifted for a few seconds. The fifth occlusion also lasted two minutes. There was some lifting of the left foreleg and a tendency of the dog to pull away. At autopsy the ligature was found around the ramus descendens, 12 mm. from the aortic origin of the left coronary artery.

PROTOCOL 3 (dog 274-43).—In about three hours the animal had recovered consciousness and was alert and active. The duration of the first occlusion was one minute. A few seconds after application of traction, the animal became restless, kicking with his left hindleg and left forepaw. He whined and threw his head about. These signs disappeared immediately after release of the ligature. A short time after this, the artery was occluded for one minute, restlessness and a shifting of the left foreleg and hindleg being produced. The next occlusion lasted one minute. A few seconds after occlusion the dog became restless moving all four legs. There were some whining and tossing the head about. None of the signs persisted after the occlusion was released. At autopsy the ligature was found around the ramus descendens, 1.8 cm. from the origin of the left coronary artery.

PROTOCOL 4 (dog 287-43).—The dog recovered full consciousness in about two hours. Occlusion for one minute was followed by yelping, and the animal became restless and tried to change his position. All these signs disappeared immediately on release of the occlusion. After a rest period, an occlusion lasting

one minute was produced. Slow grunting respirations followed but stopped as the ligature was released. A third period of occlusion lasting one minute immediately produced restlessness, and respirations became moderately labored. After a recovery period, a fourth occlusion lasting one minute produced restlessness and the respirations became grunting in character. These signs lasted for only thirty seconds, after which the animal seemed comfortable in spite of the fact that traction was maintained for a full minute. The fifth occlusion, lasting one minute and thirty seconds, resulted in restlessness and a tendency to pull away. At autopsy, the ligature was found around the ramus descendens, 1.5 cm. from the aortic origin of the left coronary artery.

PROTOCOL 5 (dog 295-43).—About three hours after the operation had been completed, the animal was fully recovered from the anesthetic. Occlusion for one minute resulted in grunting respirations. The animal became restless and pulled away, with stiffening of the left foreleg. At the release of traction, all signs disappeared. After a recovery period, occlusion for one minute produced slight restlessness and respirations became more labored. The third occlusion lasted one minute. Again there was an immediate change, respirations becoming slower and grunting in character. This was associated with pronounced restlessness. These signs disappeared promptly with the release of the ligature. At autopsy the ligature was found around the ramus descendens, 1.5 cm. from the aortic origin of the left coronary artery.

PROTOCOL 6 (dog 297-43).—In about three hours the dog had completely recovered from the anesthetic. The artery was occluded for one minute. The animal became restless and had to be held down. Respirations became much slower throughout the period of occlusion, and the dog remained tense. The struggling at the beginning of the occlusion lasted only about ten seconds. As soon as the traction was released, all signs disappeared. After a recovery period, the second occlusion, lasting two minutes, produced no change except a slight slowing of respiration. The third occlusion was maintained for one minute. There was no change for five seconds; then there was mild struggling, lasting ten to fifteen seconds. During the last thirty seconds, the animal demonstrated no signs of pain. At autopsy the ligature was found around the ramus descendens, 1.7 cm. from the aortic origin of the left coronary artery.

PROTOCOL 7 (dog 300-43).—The dog recovered consciousness and was in poor general condition three hours after operation. Occlusion of the coronary artery for thirty seconds produced no change in the demeanor or activity of the dog. After a rest period, the artery was occluded for one minute. There was no change except a slowing of respirations. The next occlusion was maintained for two minutes. Again no changes were observed except minor ones in respiration. The lack of more dramatic responses in this dog may be due to his poor condition. There were subcutaneous emphysema and considerable pneumothorax. At autopsy the ligature was around the ramus descendens, 1.8 cm. from the aortic origin of the left coronary artery.

PROTOCOL 8 (dog 303-43).—Three hours after operation the dog was in fairly good condition and conscious. Occlusion of the coronary artery for thirty seconds immediately produced stretching of the left foreleg. The dog became restless and tried to move. Respirations tended to become slower and deeper. After a recovery period, a second occlusion lasting thirty seconds immediately resulted in respiratory changes. The animal became slightly restless and scratched with his back legs at the left foreleg. The third occlusion of thirty seconds' duration resulted in immediate respiratory changes and stretching of the right foreleg. There were slight changes



in the position of the head. The pupils were dilated. The fourth occlusion lasting thirty seconds brought forth only respiratory changes. At autopsy the ligature was around the ramus descendens, 1.8 cm. from the aortic origin of the left coronary artery.

PROTOCOL 9 (dog 305-43).—The dog made a good recovery from the operation and was fairly active in his cage three hours later. Five seconds after occlusion of the coronary artery by traction on the ligature, both strands of the ligature parted. In this short interval the animal exhibited a dramatic response. He whined loudly and became extremely restless, having to be held down. All this subsided as the ligature parted. At autopsy the ligature was around the ramus descendens, 1.2 cm. from the aortic origin of the left coronary artery.

PROTOCOL 10 (dog 306-43).—Three and one-half hours after operation the dog was conscious and in a fairly good condition. Traction on the ligature for thirty seconds immediately produced movements of the left foreleg and restlessness, which was pronounced for the first ten seconds and then subsided. There was some whining fifteen seconds after the beginning of the occlusion. Respiratory changes were recorded. All signs disappeared when traction was released. After

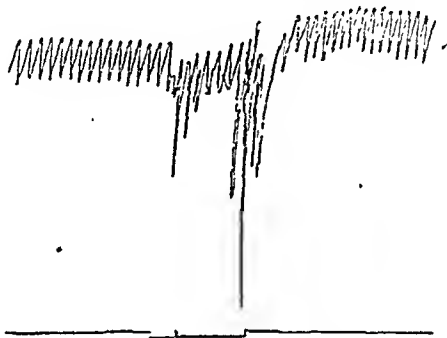


Fig. 2 (dog 306-43).—A typical tracing of the respiratory changes observed during traction on the coronary ligature in the control group of dogs. The period of traction is indicated by the break in the base line.

a rest period, the second occlusion of the artery was maintained for thirty seconds. During the first ten seconds the animal showed no changes. Then he started to move his left foreleg and became restless. Fifteen seconds after the beginning of the traction he got up and had to be restrained. These signs subsided shortly after release. The third occlusion was maintained for thirty seconds. Ten seconds later the animal was stretching the left foreleg and both back legs. The fourth occlusion lasted thirty seconds. Five seconds after the beginning of occlusion, the animal started to move his head. Twenty-five seconds later he became restless and attempted to get up. The animal immediately became quiet when traction was released. At autopsy the ligature was around the ramus descendens, 0.8 cm. from the aortic origin of the left coronary artery.

*Summary.*—Ten dogs were used in this series. Seven gave responses of a high degree, which were graded 3 plus; 2 gave fairly good positive responses (2 plus), and 1 did not respond (1 minus). In the last, the negative result was obviously partly if not totally due to the poor condition of the animal at the time of the test.

*Group II (Dogs Prepared in Advance by Pericoronary Neurectomy).*

—The animals were anesthetized with intratracheal ether or pentobarbital sodium intravenously, and respirations were maintained mechanically. The heart was exposed through a partial resection of the third and fourth left ribs. The pericardial sac was opened. The left lung was reflected downward and maintained in position by a Mikulicz pad. A small piece of moist cotton was inserted under the left auricular appendage to maintain the latter away from the operative field. The pulmonary artery was freed from the aorta at the base of the heart and reflected to the right. The space between these two vessels was well exposed by careful dissection. All the nerve branches emerging from this area and coursing along either the coronary vessels or the myocardium itself were resected over a length of 10 to 15 mm. The epicardial tissue over the left coronary artery was incised and resected from the origin of the vessel down to a few millimeters below the bifurcation. Nerve branches



Fig. 3 (dog 302-43).—A typical tracing of the respirations observed during traction on the coronary ligature in the group of dogs prepared in advance by pericoronary neurectomy. The period of traction is indicated by the break in the base line.

emerging from the posterior aspect of the aorta and coursing along the left coronary artery were resected. Afterward, the left coronary artery, being well freed from its bed, was gently scraped and phenolized. The pericardium was closed. The chest was sutured after aspiration. Electrocardiograms were taken before and after operation.<sup>12</sup>

These dogs were kept for a period of approximately one month. Then, during a second operation, the ramus descendens was exposed and prepared for the cardiac pain test, as in the first group. The group of dogs with pericoronary neurectomy were prepared by M. Fanteux, and the pain experiments of both groups were carried out by O. Swensen.

PROTOCOL 1 (dog 299-43).—One month after pericoronary neurectomy, the animal, which had been in excellent condition since the operation, was prepared for the pain test. Three hours after the second operation the animal was alert and moving around the cage. The periods of occlusion of the coronary artery, lasting one minute, thirty seconds and forty seconds, with rest periods between, were performed, with no changes in the animal. At autopsy the ligature was around the ramus descendens, at 2.8 cm. from the aortic origin of the left coronary artery.

PROTOCOL 2 (dog 302-43).—Thirty-five days after pericoronary neurectomy, the animal, which had been in excellent condition since the operation, was prepared for the pain test. Three hours after the second operation the dog was fairly active, moving around in his cage. Four periods of occlusion, each of thirty seconds'

12. These will be reported in a separate communication.

duration, resulted in no changes in the animal. At the end of the last period of occlusion, the vessel divided and there was a large amount of bleeding through the cannula. This did not seem to disturb the animal. He was killed. At autopsy the ligature was around a large vessel, which proved to be the first branch of the ramus descendens. This branch was emerging from the ramus descendens, 2 cm. from the aortic origin of the left coronary artery.

PROTOCOL 3 (dog 313-43).—Thirty-one days after pericoronary neurectomy, the animal, which had been well since operation, was prepared for the pain test. Three hours later, he was active in his cage. Traction was applied during thirty seconds. There was no change in the position or demeanor of the dog. A rest period followed. There was a second period of traction during thirty seconds. The dog showed no change whatsoever except at the end, when he moved, changing his position slightly. A rest period was followed by a third period of traction for thirty seconds. Again there was no sign of discomfort. The characteristic movement of the left foreleg was absent. The behavior of this dog during the three tests was striking in comparison to the dogs in the control series. An interesting fact is that during the first traction, an attack of ventricular paroxysmal tachycardia developed, which did not produce primary ventricular fibrillation. Often these attacks after sudden coronary occlusion are followed in dogs with intact heart by primary ventricular fibrillation (fig. 4). At autopsy the ligature was around the ramus descendens, 1.5 cm. from the aortic origin of the left coronary artery.

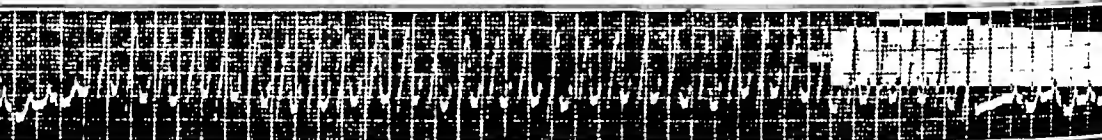


Fig. 4. (dog 313-43).—Lead II, taken during the first occlusion. Paroxysmal ventricular tachycardia is demonstrated. This was not followed by primary ventricular fibrillation, as is often the case when this rhythm develops after sudden coronary occlusion.

PROTOCOL 4 (dog 317-43).—Thirty-three days after pericoronary neurectomy, the animal, which had been in excellent condition since the operation, was prepared for the pain test. Three hours after the second operation he was conscious, being up and around his cage. Three periods of occlusion, each of thirty seconds' duration, with adequate rest periods, produced no change in the animal. The fourth occlusion lasted thirty seconds. The result this time was somewhat questionable in that at the end of the period the dog was restless. Two more periods of occlusion, each lasting thirty seconds, were carried out. The animal showed no change. At autopsy the ligature was around the ramus descendens, 1.3 cm. from the aortic origin of the left coronary artery.

PROTOCOL 5 (dog 339-43).—Thirty-one days after pericoronary neurectomy, the healthy animal was prepared for the pain test. Occlusion for thirty seconds was followed by movement of the left foreleg. A second occlusion, of forty-five seconds' duration, resulted in no change. After a rest period, the third occlusion lasted forty-five seconds. There was no change until the middle of the test, when there was a slight movement of the left foreleg. The last occlusion, of one minute's duration, resulted in no change. At autopsy the ligature was around the ramus descendens, 2 cm. from the aortic origin of the left coronary artery.

PROTOCOL 6 (dog 340-43).—Thirty-two days after pericoronary neurectomy, the well animal was prepared for the pain test. Three hours after the second operation the dog was lively and fairly normal appearing. The first occlusion lasted thirty seconds. About two seconds after occlusion there was a slight movement of the left forefoot. This was not repeated, and there were no other changes in the position of the dog. After a recovery period, a second occlusion was maintained for one minute. Five seconds after onset the animal moved. He again moved, about fifty seconds later. No other signs were noted. It must be said that this animal was extremely active and it was hard to make him stay still during the rest periods. It was, therefore, difficult to interpret the movements he made during occlusion of the coronary artery. At autopsy the ligature was around the ramus descendens, 2.2 cm. from the aortic origin of the left coronary artery.

PROTOCOL 7. (dog 5-44).—Thirty-six days after pericoronary neurectomy the animal was submitted to the pain test. When the experiment began, the dog was completely awake and not nervous. Three periods of occlusion, of thirty, sixty and sixty seconds' duration, with adequate rest periods, produced no change in the animal. At autopsy the ligature was around the ramus descendens, 2.1 cm. from the aortic origin of the left coronary artery.

PROTOCOL 8 (dog 8-44).—Thirty-eight days after pericoronary neurectomy, the well animal was submitted to the pain test. Three hours after operation the animal was awake and lively. The first occlusion lasted thirty seconds. The dog swayed; yet there were no movements of the legs and no struggle. There was a rest period, during which the dog was continuously moving and playful. The second occlusion, of one minute's duration, resulted in two movements of the left foreleg. The next occlusion was maintained for one minute. There was no change of behavior during this final test. At autopsy the ligature was around the ramus descendens, 1.8 cm. from the aortic origin of the left coronary artery.

PROTOCOL 9 (dog 9-44).—Thirty-nine days after pericoronary neurectomy, the animal was submitted to the pain test. At the time of the experiment, he was completely awake and active. Occlusion for thirty seconds resulted in some movement during the first ten seconds. After a rest period, the second occlusion lasted for thirty seconds. There were definite movement of the left foreleg and slowing of the respirations. The third occlusion lasted one minute and produced no change. The fourth occlusion, of one minute's duration, produced some movement of the left foreleg. At autopsy the ligature was around the ramus descendens, 1.2 cm. from the aortic origin of the left coronary artery.

PROTOCOL 10 (dog 58-44).—Forty-eight days after pericoronary neurectomy, the well animal was submitted to the pain test. At the time of the experiment, he was completely awake and active. Four periods of occlusion, the first of thirty seconds' duration and the rest of one minute's duration, produced no changes. At autopsy the ligature was around the ramus descendens, 2.1 cm. from the aortic origin of the left coronary artery.

*Summary.*—Ten dogs were used in this series. Six gave no responses at all (3 minus); 1 was irresponsive in five occlusions, and in 1 the result was questionable, because the animal seemed restless (2 minus); 2 gave doubtful reactions; they were active during the rest periods, and it is difficult to conclude whether the activity they presented during the tests was due to pain or whether it was just normal behavior. Only 1 had a positive reaction, which was graded 1 plus.

## COMMENT

It is generally agreed that the nerve fibers carrying pain impulses from the heart and coronary blood vessels follow the course of the coronary vessels. Woolard<sup>13</sup> has shown that the nerves to and from the ventricles are concentrated for the most part around the coronary vessels, forming a loose spiral network, and that they congregate for the most part around the origins of the coronary arteries before passing over to plexuses located between the pulmonary artery and the aorta and on the anterior surface of the aorta. Katz and Saphir<sup>14</sup> stimulated the nerve plexus between the aorta and the pulmonary artery. They found that both pressor and depressor fibers are present in this plexus and that the concentration of the afferent fibers forms a sort of "internal capsule," which they say may be important for other types of afferent fibers, such as those carrying pain. When the plexus was cauterized, the reflexes were abolished in the three experiments in which it was done. Sutton and Lueth<sup>8</sup> painted the wall of the ramus descendens of the left coronary artery with alcohol in four experiments and then repeatedly occluded the artery by pulling on the ligature, without producing pain. They considered that the pain fibers involved in experimental occlusion of the coronary artery are the nerve fibers that are found in the adventitia of the coronary artery or in the immediate surrounding tissues and that the cutting of this pathway prevents the transmission of pain. Mayne and Katz<sup>15</sup> were among the first to recognize the importance of interrupting the pain fibers as near the heart as possible not only for the essential reason of not missing any but for the purpose of avoiding the severance of important nerve branches to the lungs, which is not without certain serious risks.<sup>16</sup> They sectioned the nerve plexus in the posterior mediastinum of the dog in three experiments. It was found that traction on the ligature around the coronary vessel gave no more effective response, although stimulation of the somatic sensory nerve gave the usual response.

Our experimental results are in accordance with those of the aforementioned workers. Pericoronary neurectomy when technically well done

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13. Woolard, H. H. J.: The Innervation of the Blood Vessels, *Heart* **13**:319, 1927.

14. Katz, L. N., and Saphir, O.: The Nerve Plexus Between the Aorta and Pulmonary Artery, *Am. J. Physiol.* **104**:253, 1933.

15. Mayne, W., and Katz, L. N.: Observations on the Path Taken by the Pain Fibers from the Heart, *Am. J. Physiol.* **114**:688, 1936; Katz, L. N.; Mayne, W., and Weinstein, W.: Presence of Pain Fibers in the Nerve Plexus Surrounding the Coronary Vessels, *Arch. Int. Med.* **55**:760 (May) 1935.

16. Cromer, S. P., and Ivy, A. C.: Respiratory Death from Central Vagus Stimulation After Removal of Stellate Ganglia, *Am. J. Physiol.* **104**:457, 1933. Cromer, S. P.; Young, R. H., and Ivy, A. C.: On the Existence of Afferent Respiratory Impulses Mediated by the Stellate Ganglia, *ibid.* **104**:468, 1933.

abolishes pain. Furthermore, it has the advantage of avoiding section of nerve pathways to other vital structures. Careful observation of more than 50 dogs operated on has demonstrated to one of us (M. F.) that the operation is harmless to cardiac functions. The heart apparently can still adapt itself to the strains of increased activity. Finally, the results obtained in 2 patients<sup>17</sup> who were treated by pericoronary neurectomy combined with ligation of the great cardiac vein seem to be identical to the experimental results reported in this paper and seem to substantiate the view acquired in experimental work that pericoronary neurectomy is not deleterious to the cardiac functions. One was operated on Sept. 11, 1944. The other was operated on June 6, 1945. Both were experiencing pain at the slightest exertion and were unable to work. The first patient has never presented anginal pains since the operation, and he is now working every day, showing that this operation not only blocked the fibers carrying pain sensation but seemed to improve the cardiac function. The second patient has not been permitted to resume his work as yet. However, it is gratifying to note that he can go up and down the stairway four and five times a day and walk on the street for a long distance without experiencing any discomfort. We are well aware that it is too early to reach any final judgment regarding this new procedure; yet the experimental and clinical results seem to justify further clinical trial.

#### SUMMARY

1. Experiments carried on to test the effectiveness of pericoronary neurectomy in abolishing anginal pains in coronary disease are reported and discussed.
2. The experimental results obtained show that this procedure abolishes the signs which are considered reactions to pain in dogs submitted to the test originally described by Sutton and Lueth.
3. Clinical results in 2 patients treated by pericoronary neurectomy combined with ligation of the great cardiac vein seem to confirm the experimental findings.

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17. Since the time of submission of this communication, 7 additional patients have been treated by this operation.

# INTRAPERITONEAL ADMINISTRATION OF SUCCINYLSULFATHIAZOLE AND PHTHALYLSULFATHIAZOLE

Their Use in the Prophylaxis and Treatment of Peritonitis

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AND

WARREN H. COLE, M.D.

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SHORTLY after the introduction of the sulfonamide drugs as antibiotics, they were used intraperitoneally as a prophylaxis against peritonitis. Innumerable reports indicated that they were effective, but most surgeons abandoned their intraperitoneal use when penicillin was made available, because it appeared to be more effective than the sulfonamide compounds. Of these two drugs penicillin appears definitely to be more helpful against colon bacilli, but neither can be classified as being extremely effective against these organisms. Although streptococci and other pyogenic bacteria are occasionally isolated as causative organisms in peritonitis *Escherichia coli* is much commoner and even when a mixed infection occurs it is usually the predominant organism. Therefore, in the treatment or prophylaxis of peritonitis there would appear to be a need for an antibiotic agent which would be more effective against *Esch. coli*.

The introduction of the oral use of succinylsulfathiazole in 1941 by Poth and Knotts<sup>1</sup> and, later, phthalylsulfathiazole in 1943 by Poth and Ross<sup>2</sup> led us to investigate the absorbability of these drugs when they were introduced intraperitoneally. Experiments performed by us, as described later, revealed the fact that they were absorbed rapidly from the peritoneal cavity, although they are absorbed only to the slightest extent when given by mouth.

Poth,<sup>3</sup> Poth and Knotts,<sup>4</sup> Streicher<sup>5</sup> and Poth and Ross<sup>6</sup> have shown that when given orally succinylsulfathiazole and phthalylsulfathiazole are capable of reducing the number of bacteria (particularly *Esch. coli*)

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Mr. Everett Hoppe gave able assistance.

Aided by a grant from Sharp & Dohme, Inc.

From the Department of Surgery, University of Illinois College of Medicine and the Illinois Research and Educational Hospitals.

1. Poth, E. J., and Knotts, F. L.: Clinical Use of Succinylsulfathiazole, *Arch. Surg.* **44**:208 (Feb.) 1942.

2. Poth, E. J., and Ross, C. A.: Phthalylsulfathiazole, a New Bacteriostatic Agent, *Federation Proc.* **2**:89, 1943.

(Footnotes continued on next page)

in the feces to a remarkably low number. This has led to a rather widespread oral use of these drugs in colonic surgery. Large doses of the drugs have been administered, without detectable damage to the laboratory animals or to the patients. This has been thought to be merely a reflection of one of the physical properties of the drugs, namely, the low rate of absorption from the gastrointestinal tract. Per gram of drug, phthalylsulfathiazole is about twice as effective as succinylsulfathiazole. Toxic manifestations have been minimal or entirely absent in patients receiving 0.15 to 0.25 Gm. of succinylsulfathiazole or 0.08 to 0.12 Gm. of phthalylsulfathiazole per kilogram of body weight by mouth per day.

#### EXPERIMENTS ON ANIMALS

*Succinylsulfathiazole.*—We made a sterile suspension of succinylsulfathiazole in isotonic solution of sodium chloride and, under sterile precautions, injected (with a syringe and needle) 0.25 Gm. of the drug per kilogram of body weight into the peritoneal cavities of 8 dogs. Samples of blood were taken every four hours for thirty-two hours. As shown in the chart (*A*), the maximum level (2.5 mg. per hundred cubic centimeters) was noted at four hours.

None of the dogs evinced signs of toxicity. One dog was explored at the end of twenty-four hours to allow inspection of the peritoneal cavity. There were small clumps of the drug on the folds of mesentery, and this was estimated to represent about 20 per cent of the quantity of the drug placed therein. There was only a moderate amount of peritoneal fluid, and there was no evidence of peritoneal irritation. The incision was closed, and the animal recovered without further difficulty.

The abdomen of a second dog was opened at the end of forty-eight hours and the peritoneal cavity inspected. The succinylsulfathiazole had been completely absorbed, and again there were no signs of irritation. There were a few fibrinous adhesions between the omentum and the site of the needle puncture.

The remaining 6 dogs were operated on at intervals up to twenty-one days and similar observations made. No trace of the drug could be found; likewise, peritoneal irritation was absent or minimal.

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3. Poth, E. J.: The Sulfonamides as Therapeutic Agents in Intestinal Antisepsis: Collective Review, *Internat. Abstr. Surg.* **78**:373, 1944; in *Surg., Gynec. & Obst.*, May 1944; Succinylsulfathiazole: An Adjuvant in Surgery of the Large Bowel, *J. A. M. A.* **120**:265 (Sept. 26) 1942.

4. Poth, E. J.; Knotts, F. L.; Lee, J. T., and Inui, F.: Bacteriostatic Properties of Sulfanilamide and Some of Its Derivatives: I. Succinylsulfathiazole, a New Chemotherapeutic Agent Locally Active in the Gastrointestinal Tract, *Arch. Surg.* **44**:187 (Feb.) 1942.

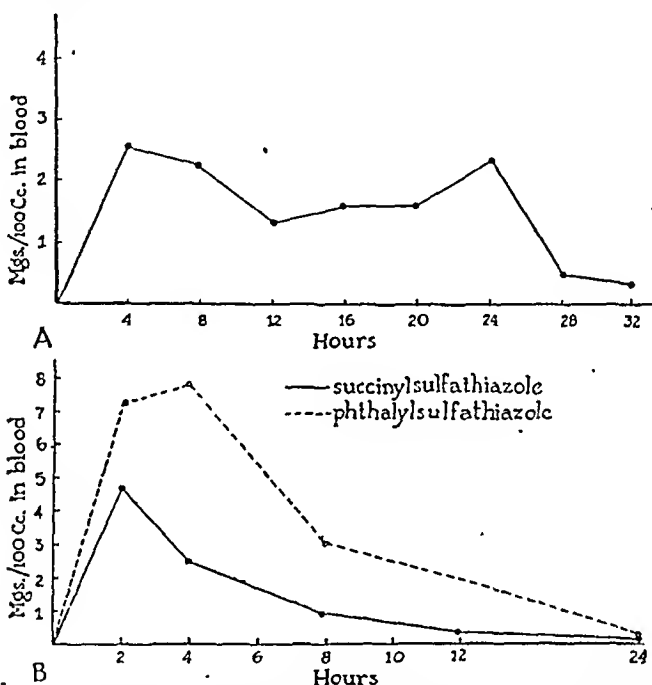
5. Streicher, M. H.: Phthalylsulfathiazole, *J. A. M. A.* **129**:1080 (Dec. 15) 1945.

6. Poth, E. J., and Ross, C. A.: The Clinical Use of Phthalylsulfathiazole, *J. Lab. & Clin. Med.* **29**:785 (Aug.) 1944.



Dog 1 was reoperated on at thirty days, and no evidence of damage to the peritoneal cavity was found. Dog 2 was likewise reoperated on at fourteen days, and similar results were noted.

In order to study the toxic effects of massive doses of succinylsulfathiazole, we injected 5 Gm. of the drug per kilogram of body weight into the peritoneal cavities of 2 dogs. Both were dead in thirty-six hours. Histologic studies revealed diffuse pneumonitis throughout both lungs. There was about 300 cc. of yellow fluid in the peritoneal cavity. No drug crystals were demonstrable in the kidney.



*A*, blood level of sulfathiazole after intraperitoneal injection of 0.25 Gm. per kilogram of body weight of succinylsulfathiazole in the dog. The graph represents the average of 8 dogs. Note that the blood level is lower but maintained longer than with the smaller dose used in human beings (see *B*). *B*, blood level of sulfathiazole after implantation of 0.1 Gm. per kilogram of body weight of succinylsulfathiazole, as compared with the level following implantation of phthalylsulfathiazole into the peritoneal cavity of human beings at the time of operation. Each graph represents the average in 12 patients.

Into a series of 8 dogs 2.5 Gm. of the drug per kilogram of body weight was injected intraperitoneally. Three of the 8 dogs vomited within one hour after injection, but at no time did they appear acutely ill. One dog died nine days later, and at autopsy it was apparent that the liver and small bowel had been punctured at the time of injection. The dog had struggled violently while the needle was in place, and from the second day on he appeared listless and failed to eat as well as the other dogs under study. There was a walled-off cavity containing about 30 cc. of bile-stained fluid, and there was a localized

abscess about a loop of ileum. Dissection revealed a small hole in the wall of the bowel. The peritoneum was covered with a fibrinous exudate.

The remaining 7 dogs were killed at intervals up to thirty days. There was no evidence of peritoneal irritation in any of the dogs, and the histologic studies did not reveal parenchymal damage to any of the visceral organs.

*Phthalylsulfathiazole*.—Into the peritoneal cavities of 4 dogs 5 Gm. of phthalylsulfathiazole per kilogram of body weight was injected as a suspension in isotonic solution of sodium chloride. All 4 dogs vomited within thirty minutes; 2 dogs died within twenty-four hours. Autopsies revealed approximately 300 cc. of yellow peritoneal fluid and diffuse hyperemia of all parenchymatous organs. About 25 per cent of the drug injected was found well distributed throughout the peritoneal cavity.

Six dogs were given 2.5 Gm. of phthalylsulfathiazole intraperitoneally per kilogram of body weight. All 6 dogs vomited within thirty minutes. Two dogs died within twenty-four hours, but the other 4 dogs remained alive and after their initial vomiting seemed to suffer no evil effects.

Four dogs were given 1 Gm. of the drug per kilogram of body weight intraperitoneally. All the dogs vomited but remained alive and well. Two dogs were killed, 1 at seven and another at fourteen days, and histologic sections of the visceral organs were studied. Aside from a mild hyperemia at seven days, no pathologic changes were noted.

#### INTRAPERITONEAL USE OF THE DRUGS IN HUMAN BEINGS

In a clinical study of the intraperitoneal use of succinylsulfathiazole and phthalylsulfathiazole,<sup>7</sup> a dose was adopted which would be no greater than 0.1 Gm. per kilogram of body weight. Since animals tolerated a dose of at least 1 Gm. per kilogram of body weight, given intraperitoneally, without any evidence of toxic reaction with either drug, the dose of 0.1 Gm. per kilogram of body weight for human beings would appear to be entirely safe.

Up to date we have used succinylsulfathiazole in 28 patients and phthalylsulfathiazole in 23 patients intraperitoneally<sup>8</sup> in a dose of 6 Gm. for an adult, which is approximately 0.1 Gm. per kilogram of body weight. The drug has been dusted in as a powder or suspended in 20 to 30 cc. of isotonic solution of sodium chloride and poured into the peritoneal cavity. Care must be taken lest the drug get into the wound,

7. We are informed by Dr. M. Streicher of Chicago that he has also used both of these drugs intraperitoneally as a prophylaxis against postoperative peritonitis.

8. The drugs were sterilized by heating in a dry oven for four hours at a temperature of 140 C.

since experiments on animals conducted by one of us (J. Y.) have shown that its presence in a wound will delay healing. This is to be expected since neither of the two drugs, unlike other sulfonamide compounds, is absorbed from subcutaneous tissue.

The patients were watched carefully postoperatively for signs of toxic manifestations, such as hematuria, oliguria, leukopenia, agranulocytosis, nausea, vomiting, headache and mental confusion; specimens of blood were drawn at specified intervals up to twenty-four hours for determinations of blood levels. In none of the patients did we observe any evidence of toxic reaction to either of the two drugs; results of urinary examinations also were consistently normal.

Two cases were of particular interest to us since they gave us an opportunity to study the effect of phthalylsulfathiazole on established peritonitis. One of the patients was a Negro boy, 10 years old, who entered the Research and Educational Hospitals with a history of abdominal pain of five days' duration. Examination revealed general peritonitis arising from a perforated appendix. He had been treated at home with catharsis and enemas, and at the time he entered the hospital he was irrational, dehydrated, toxic and almost preterminal. Since children with perforated appendixes respond so poorly to conservative or delayed surgical treatment, it was thought that operation should be performed as soon as dehydration and electrolyte imbalance could be corrected. After several hours of preoperative treatment, operation was performed; the appendix was removed and an abscess drained although it was obvious that general peritonitis also existed. Culture revealed *Esch. coli*, hemolytic *Staphylococcus aureus* and a nonhemolytic streptococcus. Four grams of phthalylsulfathiazole was placed in the peritoneal cavity. The administration of penicillin, which had been started preoperatively in doses of 30,000 units every three hours, was continued. The patient died four days later, and at autopsy the peritoneal exudate was again cultured. The cultures revealed numbers of hemolytic *Staph. aureus* and nonhemolytic streptococci, but no *Esch. coli* were found. Another patient illustrated the same point, namely, disappearance of *Esch. coli* in the peritoneal cavity following implantation of phthalylsulfathiazole into the peritoneal cavity, although streptococci and staphylococci were still present on culture. In a Negro woman, aged 23 years, a spontaneous perforation of the cecum developed at the site of a tuberculous ulcer. At operation, which was delayed twelve hours because of the patient's refusal to give permission for operation, there was generalized peritonitis along with disseminated tuberculous peritonitis. The perforated cecum was exteriorized, and 6 Gm. of phthalylsulfathiazole was implanted in the peritoneal cavity before closure. Culture of material taken at the time of operation revealed *Esch. coli*, streptococci and staphylococci. Roentgenologic examination of the chest revealed

minimal tuberculosis of the lungs. At autopsy, three days later, which confirmed the operative findings, culture revealed no *Esch. coli* but numerous colonies of streptococci and staphylococci. The patient had been given heavy doses of penicillin (300,000 units per day) beginning with the date of operation.

We admit that no conclusions can be drawn from these cases, but since penicillin is known to be much less effective against colon bacilli than against pyogenic organisms one would be inclined to attribute the elimination of the infection with colon bacilli to the phthalylsulfathiazole rather than to penicillin, particularly since we know that it is so effective against that organism in the intestinal tract. However, it is important to note that intensive penicillin therapy failed to eliminate the streptococci and staphylococci in both instances.

#### ANALYSIS OF RESULTS

In clinical trials on human beings as well as in experiments on dogs, we noted that succinylsulfathiazole and phthalylsulfathiazole were absorbed rapidly from the peritoneal cavity. The peak blood level occurs within the first few hours after implantation.

In none of the patients receiving the drugs in the dose of approximately 0.1 Gm. per kilogram of body weight was there any evidence of toxic reaction. Routine urinary examinations revealed no albumin, red blood cells, crystalluria or any other pathologic change. This freedom from abnormal urinary findings is perhaps explained on the basis that the kidneys do not excrete large amounts of either drug (Poth and Ross<sup>9</sup>) in the free form and that the conjugated form is soluble at a  $p_H$  as low as 5.61. Nevertheless, we were careful to insure a daily fluid intake of at least 2,500 cc.

In dogs it had been determined that 2.5 Gm. of succinylsulfathiazole per kilogram of body weight could be used without serious side effects and that 1 Gm. per kilogram of phthalylsulfathiazole could likewise be used intraperitoneally with safety. Hence we felt entirely safe in using 0.1 Gm. per kilogram of body weight in human beings; subsequent observations seemed to justify that dose.

From the previous study by Walter and Cole<sup>9</sup> and others, we know that clumping of the sulfonamide drugs in the peritoneal cavity will lead to a foreign body reaction; accordingly we are careful to distribute the drug diffusely. When the drug is suspended in isotonic solution of sodium chloride, there is less danger of clumping. Neither of the two drugs studied showed any tendency to produce intra-abdominal adhesions, thereby resembling sulfanilamide; it is well known that sulfathiazole and

9. Walter, L., and Cole, W. H.: The Intraperitoneal Administration of Sulfadiazine, *Surg., Gynec. & Obst.* 76:524 (May) 1943.

sulfadiazine produce a few adhesions following implantation in the abdominal cavity, but they disappear after six to ten days.

Determinations of the blood levels of sulfathiazole in patients having 0.1 Gm. succinylsulfathiazole or phthalylsulfathiazole placed in their peritoneal cavities reveal that a peak is reached rapidly (see chart, *B*), but that the peak is maintained for only a short time. This would not appear to be entirely desirable. However, since the purpose of implantation of a sulfonamide drug into the peritoneal cavity is to combat soilage incurred at the time of operation and could not be expected to offer much protection against a leaking suture line, which usually occurs only after a few days, perhaps the need for prolonged exposure is not so urgent. From the standpoint of slow absorption sulfadiazine and sulfathiazole are superior to the two drugs being discussed, but since these two drugs are so ineffective against *Esch. coli* they have been supplanted by penicillin. Some authors have reported penicillin to be mildly effective against *Esch. coli*, but our experience with penicillin in *Esch. coli* infections has been disappointing. Preliminary reports concerning streptomycin are encouraging in infections with colon bacilli; it is therefore possible that this drug given along with penicillin would eliminate indications for intraperitoneal implantation of any drugs.

That phthalylsulfathiazole is effective against colon bacilli in the peritoneal cavity is suggested by histories of 2 cases discussed previously in this report. Penicillin had failed to eliminate the staphylococci and streptococci from the peritoneal exudate in both cases, but the colon bacilli had been eliminated; we are inclined to attribute this effect on the colon bacilli to phthalylsulfathiazole and not to penicillin.

Because of the preliminary nature of this report, we have not attempted to evaluate the efficacy of succinylsulfathiazole or phthalylsulfathiazole in reducing postoperative peritonitis or other complications. In view of the low incidence of postoperative peritonitis in carefully performed intestinal anastomoses, it will be necessary to study several hundred cases before definite conclusions can be reached on this point.

#### SUMMARY

When succinylsulfathiazole and phthalylsulfathiazole are implanted in the peritoneal cavities of human beings or dogs, they are rapidly absorbed into the blood stream; the average peak level of the two drugs at four hours was 4 versus 5 mg. per hundred cubic centimeters respectively (see chart, *B*). The rate of disappearance from the peritoneal cavity is much more rapid than that of sulfathiazole or sulfadiazine and resembles more closely the rate of disappearance of sulfanilamide. Adhesions of the type which are encountered experimentally for several days after intraperitoneal implantation of sulfadiazine and sulfathiazole (but which later disappear) are not observed after use of either drug.

Either of the drugs herein discussed can be given intraperitoneally to dogs in a dose of at least 1.0 Gm. per kilogram of body weight, without reaction. We have adopted a dose of 0.1 Gm. per kilogram of body weight for human beings, but, in view of the low toxicity in animals, it would appear that the dose could be increased in human beings over that which we used; we noted no toxic reactions of any type in any of the patients to whom the drug had been given.

Our series of cases is too small to allow us to compare it with a control series, since the incidence of significant postoperative intraperitoneal infection which this therapy would hope to prevent is too small to allow comparison unless several hundred cases were studied. However, since both drugs are known to be extremely effective in reducing the *Esch. coli* count of the stool when they are given orally, it might be reasonable to suppose that they would also be effective against that same organism occurring as a contaminant following intestinal resection.

We are unable to predict which of the two drugs would be the more effective, but since the blood level following a given dose of each is slightly higher and more prolonged with phthalylsulfathiazole this drug might be expected to be more effective than succinylsulfathiazole.

## LYMPHADENOID GOITER

Its Differentiation from Chronic Thyroiditis

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AND

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WHILE in recent articles (Joll,<sup>1</sup> Graham,<sup>2</sup> Hellwig,<sup>3</sup> McSwain and Moore<sup>4</sup> and Schilling<sup>5</sup>) lymphadenoid goiter is recognized as a pathologic and clinical entity, the causes, histogenesis and clinical significance of this rare form of goiter are still little understood.

Since 1940, we have had the opportunity of observing 14 cases of lymphadenoid goiter. We are presenting the histologic data because we found alterations of the thyroid epithelium which have not been correctly interpreted in recent studies, and we believe that these epithelial changes, rather than the more conspicuous accumulations of lymphoid tissue, are the most important characteristics of this disease.

### CLINICAL FINDINGS

The 14 patients were all women. While 2 patients were 16 and 27 years old respectively, the ages of all others ranged from 32 to 61 years, the average age being 44.7 years. The patients had noticed, from six weeks to twenty years previous to admission to the hospital, the following symptoms: 13 complained of enlargement of the thyroid, with or without pressure symptoms; 11 had noticed nervousness; 2 had rapid heart rates, 1 had sweating and tremor of the hands, and 1 had lost some weight.

Regarding sex life, the following data are of interest. Twelve of our patients were married, and 7 had from one to four children. Only 3 of the 14 patients had regular menses, 6 were in the menopause, 2 complained of dysmenorrhea and 1 had irregular periods. Physical examina-

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From the Department of Pathology, St. Francis Hospital.

1. Joll, C. A.: The Pathology, Diagnosis and Treatment of Hashimoto's Disease (Struma Lymphomatosa), *Brit. J. Surg.* **27**:351, 1939.

2. Graham, A., and McCullaugh, E. P.: Atrophy and Fibrosis Associated with Lymphoid Tissue in the Thyroid, *Arch. Surg.* **22**:548 (April) 1931.

3. Hellwig, C. A.: Lymphadenoid Goiter, *Arch. Path.* **25**:838 (June) 1938.

4. McSwain, B., and Moore, S. W.: Struma Lymphomatosa, *Surg., Gynec. & Obst.* **76**:562, 1943.

5. Schilling, J. A.: Struma Lymphomatosa, Struma Fibrosa and Thyroiditis, *Surg., Gynec. & Obst.* **81**:533, 1945.

*Clinical and Pathologic Findings*

| Case | Age, Yr. | Duration | Menses              | Gynecologic Surgery | Clinical Diagnosis     | Weight of Thyroid, Gm. | Gross Appearance | Stroma   | Lymphocytes, per Cent | Colloid | Adnl  | Hürthle Cells |
|------|----------|----------|---------------------|---------------------|------------------------|------------------------|------------------|----------|-----------------------|---------|-------|---------------|
| 1    | 41       | 2.5 yr.  | Normal              | None                | Fetal adenoma          | 42                     | Diffuse          | Seanty   | 40                    | Seanty  | Small | Many          |
| 2    | 27       | 6 yr.    | Dysmenorrhea        | None                | Nontoxic goiter        | 50                     | Diffuse          | Seanty   | 20                    | Seanty  | Small | Many          |
| 3    | 50       | 2 yr.    | Surgical menopause  | Hysterectomy        | Colloid goiter         | 66                     | 2 nodes          | Seanty   | 25                    | Some    | Small | Many          |
| 4    | 40       | 1 yr.    | Beginning menopause | None                | Nodular colloid goiter | 70                     | 2 nodes          | Seanty   | 10                    | Seanty  | Small | Many          |
| 5    | 30       | 3 yr.    | Dysmenorrhea        | None                | Nodular colloid goiter | 44                     | Diffuse          | Seanty   | 50                    | Some    | Small | Many          |
| 6    | 58       | 15 yr.   | Menopause           | None                | Colloid goiter         | 50                     | Diffuse          | Seanty   | 40                    | Some    | Small | Many          |
| 7    | 32       | 7 mo.    | Irregular           | None                | Diffuse colloid goiter | 41                     | Diffuse          | Seanty   | 40                    | Seanty  | Small | Some          |
| 8    | 36       | 5 wk.    | .....               | None                | Nodular colloid goiter | 60                     | 2 nodes          | Seanty   | 20                    | Some    | Small | Many          |
| 9    | 47       | 7 yr.    | Menopause           | Pelvic tumor        | Fetal adenoma          | 27                     | Diffuse          | Moderate | 60                    | Seanty  | Small | Few           |
| 10   | 61       | 15 yr.   | Menopause           | Hysterectomy        | Nodular toxic goiter   | 30                     | 1 node           | Moderate | 60                    | None    | Small | Great many    |
| 11   | 16       | 1 yr.    | .....               | Brain tumor         | Toxic goiter           | 28                     | 2 nodes          | Seanty   | 50                    | Some    | Small | Many          |
| 12   | 38       | 2 yr.    | Normal              | Salpingectomy       | Toxic goiter           | 24                     | Diffuse          | Much     | 50                    | Some    | Small | Few           |
| 13   | 36       | 20 yr.   | Normal              | Caesarian section   | Toxic goiter           | 42                     | Diffuse          | Seanty   | 50                    | Seanty  | Small | Some          |
| 14   | 48       | ?        | Menopause           | None                | Toxic goiter           | 30                     | Diffuse          | Seanty   | 20                    | None    | Small | Some          |



tion revealed a variation in pulse rates from 64 to 88, while the blood pressures ranged from 100 to 150 systolic and 65 to 90 diastolic.

The preoperative diagnoses were nontoxic goiter in 8, fetal adenoma in 2 and toxic goiter in 4 cases. Three patients received preoperative treatment with strong solution of iodine, U. S. P., and the youngest patient had received iodine for six months previous to admission. In all the patients except 1 both lobes of the goiter were removed at operation. In only 3 patients were postoperative elevations of temperature above 101 F. observed. As a rule the patients were discharged from the hospital ten days after thyroidectomy.

Follow-up data were available from all except 2. No recurrence of the goiter was noticed. In 4 patients mild signs of decreased thyroid function appeared about six months after thyroidectomy. These symptoms were controlled satisfactorily by the administration of thyroid.

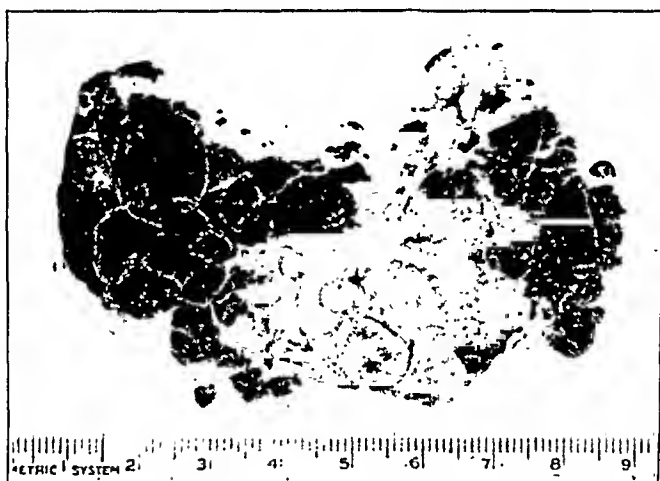


Fig. 1.—Lymphadenoid goiter (case 6). Diffuse grayish brown firm cut surface.

#### PATHOLOGIC FINDINGS

The surgical specimens weighed from 24 to 70 Gm., the average weight being 45.7 Gm. Since normal thyroids obtained in Wichita at autopsies of women in the fifth decade of life weigh 20.8 Gm. (Hellwig<sup>6</sup>), the lymphadenoid goiters represented a definite increase in weight over the normal.

The contours of the removed goiters were regular, and in only 1 case had the surgeon noticed firm adhesions to the surrounding structures. The cut surface was divided into distinct lobules, and the tissue in most specimens was uniform throughout. The tissue was light

<sup>6</sup> Hellwig, C. A.: The Thyroid Gland in Kansas, *Am. J. Clin. Path.* 5:103, 1935.

grayish brown, resembling pancreas, and had a firm consistency. In 5 cases small nodules were visible, which measured not more than 10 mm. in diameter, an incidence which conforms with our autopsy findings in normal thyroids of patients in this age group.

The microscopic pictures in our 14 cases were strikingly uniform. While the abundance of lymphoid tissue has been stressed by most observers as the most conspicuous feature, we found, by actual measurement of the lymphoid and epithelial tissue in paraffin sections, that only one third of the enlargement of the thyroid gland can be explained by proliferation of lymphoid tissue, while two thirds of the gland consisted of epithelial tissue. In our opinion, the accumulation of lymphoid tissue is a secondary phenomenon and represents a response of lymphocytes to an abnormal function and proliferation of thyroid epithelium.

Our findings on the thyroid epithelium were at variance with those of former observers and warrant more detailed consideration. Most of the acini were of small size and had oval or slitlike lumens. The epithelium was high cuboid and measured between 8 and 12 microns in height. The cytoplasm of these cells stained light bluish, and most of the cells were without evidence of degeneration. As a rule the lumens of these acini were without stained colloid but often contained groups of cells with dark nuclei and indistinct outlines. The latter have been regarded by most writers as desquamated acinar cells; however, one occasionally sees a bud of large histiocytes protruding through a defect in the acinar wall, and therefore it seems more probable that the origin of these intrafollicular cells is from wandering cells of tissue.

Foreign body giant cells attached to fragments of colloid or tubercle-like structures, which are common in chronic thyroiditis, were completely absent in our material.

More striking was another type of thyroid epithelium, which was present in every case of our series, namely pale large polygonal cells which resembled hepatic or adrenal cells much more than thyroid epithelium. These unusual cells were arranged either in acini with small lumens or in solid cell strands surrounded with lymphoid tissue. The size of these pale cells varied between 20 to 30 microns, their vacuolated cytoplasm took an intense stain with eosin and the nuclei were of varying size; often eccentric, they had a fine chromatin network and occasionally one or two small nucleoli.

While these large pale cells have attracted the attention of previous observers, there is disagreement in regard to their significance. Breun-  
ger<sup>7</sup> and Joll<sup>1</sup> regarded them as regenerative or hypertrophic, while the

7. Bruenger, H.: Ueber Operationstod bei Thyroiditis chronica, Mitt. a. d. Grenzgeb. d. Med. u. Chir. 28:213, 1915.



Fig. 2.—*A*, small acini without colloid. Some cells in the lumens. No degeneration of epithelium. *B*, compensatory proliferation of large pale oxyphilic cells identical with Hürthle cells.

majority of investigators (Reist,<sup>8</sup> Graham<sup>2</sup> and Schilling<sup>5</sup>) described them as inactive or degenerated. Hertzler<sup>9</sup> ascribed a pathologic secretion responsible for myxedema to cells of this type, and he advised total thyroidectomy to get rid of these "myxedema cells."

The pale eosinophilic cells with abundant cytoplasm, so characteristic of lymphadenoid goiter, are without doubt identical with the "protoplasm rich" cells of Hürthle.<sup>10</sup> In 1894 Hürthle described them in normal human thyroids on the outer wall of follicles and stated the belief that they were immature reserve cells.

While Hürthle<sup>10</sup> himself did not observe any thyroid tumors composed of this type of cell, about 23 cases of benign and malignant Hürthle cell tumors have been reported since 1907 (Morrow<sup>11</sup>). It is of significance that with few exceptions these tumors occurred in women older than 40 years. The average age of the patients with Hürthle cell tumors reported in the literature is 45.7 years, while the average age of our patients with lymphadenoid goiter is 44.7 years. Two of the lymphadenoid goiters in our series, from women of 36 and 46 years, had small adenomas composed of Hürthle cells, and the tumor cells were of the same form, size and color as the large pale cells in the diffuse tissue of the same specimen.

There is disagreement in the literature regarding the origin of the Hürthle cells. While Getzowa<sup>12</sup> derived them from the postbranchial bodies and Eisenberg and Wallerstein<sup>13</sup> from the parathyroid glands, Wilensky and Kaufman's<sup>14</sup> explanation seems more plausible, stating that the Hürthle cell is a physiologic-pathologic variant of the thyroid cell and that it arises from normal thyroid epithelium because of metabolic or nutritional disturbances.

The fact that Hürthle cells have been found occasionally in normal thyroids of small children (Wegelin<sup>15</sup>) and in exophthalmic goiters

8. Reist, A.: Ueber chronische Thyreoiditis, Frankfurt. Ztschr. f. Path. 28:141, 1922.

9. Hertzler, A. E.: Surgical Pathology of the Thyroid Gland, Philadelphia, J. B. Lippincott Company, 1936, p. 198.

10. Hürthle, K.: Beiträge zur Kenntnis des Sekretionsvorganges in der Schilddrüse, Arch. f. d. ges. Physiol. 56:1, 1894.

11. Morrow, W. J.: Hürthle Cell Tumor of the Thyroid Gland in an Infant, Arch. Path. 40:387 (Nov.-Dec.) 1945.

12. Getzowa, S.: Ueber die Glandula parathyroidea, intrathyroidale Zellhaufen derselben und Reste des postbranchialen Koerpers, Virchows Arch. f. path. Anat. 188:181, 1907.

13. Eisenberg, A. A., and Wallerstein, H.: Hürthle Cell Tumor, Arch. Path. 13:716 (May) 1932.

14. Wilensky, A. O., and Kaufman, P. A.: Hürthle Cell Tumor of the Thyroid Gland, Surg., Gynec. & Obst. 66:1, 1938.

15. Wegelin, C., in Henke, F., and Lubarsch, O.: Handbuch der speziellen pathologischen Anatomie und Histologie, Berlin, Julius Springer, 1926, vol. 8 p. 118.

(Roussy<sup>16</sup>) and that they may give rise to benign or malignant thyroid tumors favors the view that they are young proliferating cells rather than degenerated and atrophic.



Fig. 3.—Lymphadenoid goiter with adenoma composed of Hürthle cells (case 4).

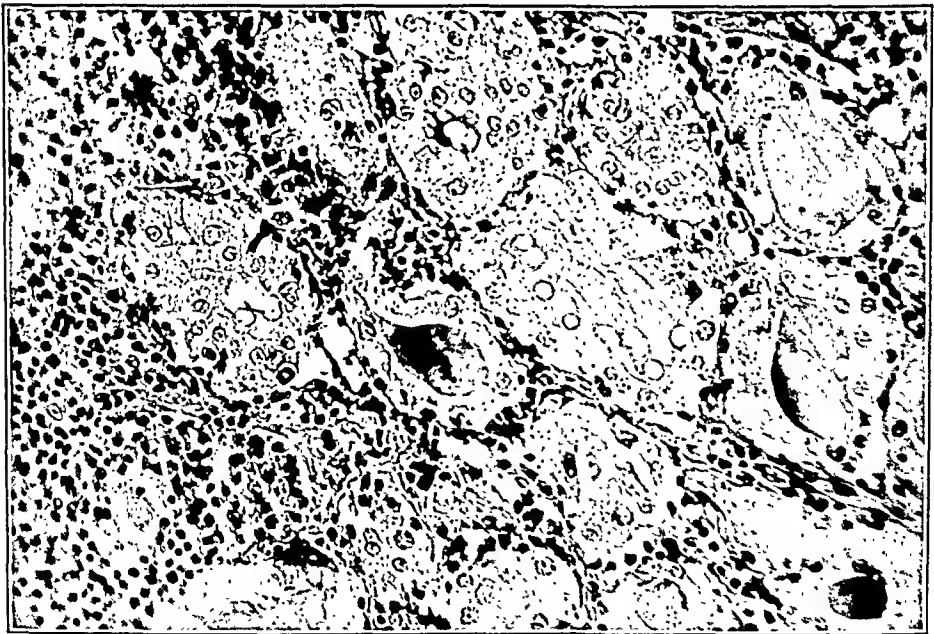


Fig. 4.—Hürthle cells in adenoma, indistinguishable from large pale oxyphilic cells of lymphadenoid goiter (compare with figure 2 B).

16. Roussy, G., in *Verhandlungsbericht*, hrsg. im Auftrag der Schweiz. Internationalen Kopfkongferenz (1933), Bern, H. Huber, 1935, vol. 2, p. 175.

The question that then presents itself is why lymphadenoid goiter in spite of epithelial hyperplasia is often associated with hypothyroidism. To answer it one has to consider the normal activity of the thyroid acinus. Microscopic observations by Williams<sup>17</sup> of the follicle of the living thyroid implanted in transparent chambers have shown that the activity of the thyroid cell is cyclic. The normal cycle consists of two phases: the colloid storage phase and the colloid release phase. During the first phase, which can be precipitated by iodine, the acinar cells actively manufacture colloid and secrete it into the lumen of the follicle, where it is stored. During the release phase, which is under the influence of thyrotropin, the colloid is resorbed from the acinar lumen into the circulation. Normal thyroid function can be maintained only when there is a balance between the two phases of the cycle—colloid secretion and colloid resorption.

Histologic and functional changes in lymphadenoid goiter indicate an interruption of the cycle. The lymphadenoid goiter has lost its faculty to manufacture colloid, and the supply of stored thyroid hormone becomes exhausted. In contradistinction to exophthalmic goiter, which promptly converts into colloid goiter after treatment with strong solution of iodine, U. S. P., even large doses of iodine are unable to restore the manufacture of colloid in lymphadenoid goiter. This explains why iodine has no value in the prevention or cure of lymphadenoid goiter.

The hyperplastic pale cells found in every lymphadenoid goiter of our series represent an attempt to compensate for the exhaustion of thyroid hormone. However, the cells are neither secreting colloid into the acinus nor resorbing it into the blood stream. The oxyphilic secretory material collects in the cytoplasm and distends the cells to a bizarre size.

It is well to remember that in experimental goiter loss of colloid and cellular hyperplasia is also associated with low thyroid function (Hellwig<sup>18</sup>). The recently discovered goitrogenic agent, thiouracil, interferes directly with the synthesis of colloid, as Astwood<sup>19</sup> has shown. By removal of the antagonistic effect of the thyroid secretion on the hypophysis, excessive production of thyrotropic hormone results. The latter stimulates the thyroid to increased colloid resorption and to epithelial hyperplasia, but the basal metabolic rate becomes low because the stored thyroid hormone becomes exhausted and there is no synthesis of colloid. Iodine is unable to restore the normal thyroid cycle, and

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17. Williams, R. G.: Microscopic Studies of Living Thyroid Follicles Implanted in Transparent Chambers Installed in the Rabbit's Ear, *Am. J. Anat.* **62**:1, 1937.

18. Hellwig, C. A.: Experimental Goiter, *Arch. Path.* **19**:364 (March) 1935.

19. Astwood, E. B.: Treatment of Hyperthyroidism with Thiourea and Thiouracil, *J. A. M. A.* **122**:78 (May 8) 1943.

administration of thyroxin is necessary to restrain the overactivity of the hypophysis.

A similar sequence of events is apparently the cause of lymphadenoid goiter, except that the thyroid cycle is not interrupted by a chemical agent, as in thiouracil goiter, but by the hyperactivity of the hypophysis following loss of ovarian function. Most lymphadenoid goiters occur in women near or during menopause. A decline of ovarian function removes the antagonistic effect on the activity of the hypophysis and increases its hormone secretion. The excess of thyrotropic hormone will, as in thiouracil goiter, produce in the thyroid loss of colloid and hyperplasia of the thyroid epithelium, but the function of the thyroid will be deficient because there is no synthesis of colloid. Iodine will not restore the normal cycle, and thyroid extract is necessary to counteract the hyperactivity of the hypophysis.

#### SUMMARY AND CONCLUSIONS

The clinical data and histologic changes in 14 cases of lymphadenoid goiter suggest that lymphadenoid goiter is a clinical and pathologic entity and that it is not an inflammatory process but the result of a disturbance of the normal cycle of thyroid activity—colloid secretion and release.

Two types of epithelial alterations were present in all our cases: (1) small slitlike acini with high cuboid epithelium and loss of colloid and (2) strands of large pale oxyphilic cells which resemble hepatic or adrenal cells. The latter are identical with the so-called Hürthle cells. Hürthle cell tumors occur almost exclusively in women over 40 years of age, as do lymphadenoid goiters. These large pale cells represent in our opinion an attempt to compensate for the exhaustion of colloid in the small slitlike acini.

Lymphadenoid goiter is explained best by a similar sequence of events as occurs in thiouracil goiter except that the disturbance of the cyclic activity of the thyroid acinus is not initiated by a chemical agent but by loss of ovarian function.

## ANAPHYLAXIS-LIKE REACTIONS PRODUCED BY ASCARIS EXTRACTS

### III. The Role Played by Leukocytes and Platelets in the Genesis of the Shock

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IN the two preceding papers<sup>1</sup> of this series we have described the main features of the shock produced in the dog by the intravenous injection of deproteinized and dialyzed extracts from *Ascaris lumbricoides*. We have shown that histamine and heparin are discharged in conspicuous amounts from liver cells when the extracts are injected into the intact animal and that glycogen inhibits this release when injected before the extracts. This effect of liver glycogen was ascribed to its capacity for reducing the number of leukocytes and platelets of circulating blood by allocating them to nonspecified organ structures all over the body. On the contrary, in anaphylactic shock or in the shock produced by *Ascaris* extracts it should be a preferential allocation of clumped leukocytes and platelets to the structure of the shock organs. As regards the rabbit, pulmonary capillaries have been shown by Dragstedt and co-workers<sup>2</sup> to retain leukocytes during in vitro anaphylactic shock. We have recently shown<sup>3</sup> that liver glycogen produces drastic reductions in the histamine content and the leukocyte and platelet counts in the rabbit and at the same time partially or totally inhibits anaphylactic shock in this species of animal. By dispersing blood elements, glycogen prevents their accumulation in rabbit lung, this apparently being a preliminary condition for development of the shock in this species of animal. As regards the dog, the liver might display similar function during anaphylactic shock, since this organ is mainly concerned in the genesis of the symptoms. There remains no doubt that an initial constriction of suprahepatic veins in the dog constitutes the deflagrating event leading to the anaphylactic shock and

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From the Butantan Institute (Porto) and the Department of Biochemistry and Pharmacodynamics, Instituto Biológico (Rocha e Silva and Andrade).

1. Rocha e Silva, M., and Graña, A.: Anaphylaxis-Like Reactions Produced by *Ascaris* Extracts: I. The Changes in the Histamine Content and the Coagulability of the Blood in Guinea Pigs and in Dogs, *Arch. Surg.* **52**:523 (May); II. The Mechanism of the Shock Induced in Dogs, *ibid.* **52**:713 (June) 1946.

2. Dragstedt, C. A.; Arellano, M. R.; Lawton, A. H., and Youmans, G. P.: *J. Immunol.* **39**:537, 1940.

3. Rocha e Silva, M.; Graña, A., and Porto, A.: To be published.



that the histamine and the heparin which appear in high amounts in the circulating blood and especially in blood in the portal vein are discharged from the liver parenchyma. Since leukocytes and platelets are sharply reduced in peripheral blood during anaphylactic shock, it might be expected that they would be retained in the internal structures of the liver, forming microthrombi, which would contribute to aggravate the circulatory stasis in the portal region. The experiments described in this paper bring direct proofs for this assumption. On the other hand, the fact that a decrease in the leukocyte-platelet count as produced by glycogen partially or totally prevents the discharge of histamine and heparin from liver cells seems to warrant the conclusion that there is a close relationship between this discharge and the accumulation of blood elements to the liver parenchyma. It is important to recall that the perfusion of the liver of sensitized dogs with Tyrode solution or defibrinated blood plus the antigen was unable to produce any appreciable discharge of histamine from liver cells.<sup>1</sup> We have therefore concluded that only the contact of the antigen with the liver cells is not enough to bring forth a liberation of histamine. In the present paper we will show that whole blood has all the constituents which are necessary to bring forth this discharge of histamine and heparin from isolated liver cells when the antigen is added to the system.

#### MATERIAL AND METHODS

The *Ascaris* extracts employed were prepared according to the procedure previously described.<sup>1</sup> The anesthetic used was a combination of morphine (10 mg. per kilogram) and liquid dial (Ciba), in the dose of 0.16 cc. per kilogram. In some cases a complement by ether was employed, in others it was deliberately avoided. In a few experiments on perfusion of the liver the animal was simply anesthetized with ether.

The perfusion of the liver was performed in the way previously described, with the difference that the blood (800 cc.) for perfusion was collected over a 3.8 per cent solution of sodium citrate (200 cc.) in a paraffined beaker. All the materials which had to enter into contact with blood were carefully paraffined, with the exclusion of rubber tubings. Before whole blood was added, the liver was perfused with 500 cc. of Tyrode solution (without calcium) to which 20 per cent of the citrate solution was added. In such conditions, leukocytes and platelets were well preserved, even after many passages through the organ. Usually, three or four passages in blank preceded the injection of the *Ascaris* material into the portal cannula. The velocity of the perfusion was maintained at a high level (150 cc. per minute) during seven or eight passages of the whole blood. Then perfusion stopped, and the retained blood was allowed to drain from the organ. Histamine in the perfusates was estimated on guinea pig ileum both directly before and after extraction by Code's method.<sup>4</sup> The discharge of an anticoagulant (heparin) was roughly estimated by a recalcification of the perfusing blood with tenth-molar solution of calcium chloride and a determination of the clotting time as usual. Platelets were counted according to the method of Fonio, and the

4. Code, C. F.: *J. Physiol.* 89:257, 1937.

figures indicate the number of platelets referred to 1 cu. mm. of the starting blood. All the smears intended for counting of platelets were stained with dilute Giemsa stain and observed at a magnification of 900 diameters.

Smears of pieces of liver, in experiments on the intact dog, were uniformly made by immersing an edge of the organ into a shallow dish filled with 3.8 per cent solution of sodium citrate and cutting with sharp scissors a small fragment of liver beneath the surface of the anticoagulant. This procedure was found necessary to avoid spontaneous aggregation of platelets, although it was verified that the aggregates never displayed more than ten or twelve elements packed together. With use of the technic described, the platelets were always uniformly distributed among the erythrocytes when the smears were made by gently rubbing the pieces of liver over microscopic slides. Only occasionally, small aggregates (of seven or ten platelets) could be observed, like those which can be found in a smear from normal blood intended for counting of platelets.

Plasma trypsin (free and total) was estimated according to the method of Iyengar<sup>5</sup> with slight modifications which will be described in a separate paper. All estimations of nonprotein nitrogen were made as usual by the micro-Kjeldahl method.

#### RESULTS

*Identity of the Shock Produced by Ascaris Extracts and Anaphylactic Shock.*—Of considerable interest is the question whether the shock developed in the dog by the injection of *Ascaris* extracts is the consequence of a primary toxic effect of those extracts or of a previous sensitization of the animal to products derived from helminths usually present in their intestinal tract. Many facts are in favor of the latter alternative. *Ascaris* extracts do not act like a primary toxin, since they are entirely nontoxic for the rabbit and almost so for the cat. Like horse serum in a sensitized animal, they do not liberate histamine from isolated dog liver perfused with Tyrode solution or defibrinated blood, in contrast to the effects produced by snake venom<sup>6</sup> and trypsin.<sup>1</sup> When injected into the unanesthetized dog, *Ascaris* extracts produce a sequence of symptoms which are common to anaphylactic shock in this species of animal, the only difference being that the symptoms have an extremely severe course. After two to three minutes, the animal presents vomiting, defecation and urination, and seven to ten minutes later it falls in lateral decubitus and stays in this position for fifteen to thirty minutes, entirely unconscious, with the pupils wide open. Frequently, death occurs during this stage; if recovery occurs, the animal shows bloody diarrhea of extreme severity for many hours. At section, the liver is dark and full of blood, the walls of the intestines are hyperemic and the lumen is filled with dark blood. Table 1 shows the condensed protocols of the experiments made on 7 dogs which received decreasing doses of the extracts.

5. Iyengar, N. K.; Sehra, K. B., and Mukerji, B.: Indian M. Gaz. **77**:348, 1942.

6. Feldberg, W., and Kellaway, C. H.: J. Physiol. **90**:257, 1937.

The analogy between the symptoms induced in the dog by the *Ascaris* extracts and those characterizing anaphylactic shock in this species of animal is so profound that one is induced to apply the observations concerning the mechanism of the former to a better understanding of the latter. It seems to us that many of the conclusions emerging from the study of the shock by *Ascaris* were rendered clearer on account of the fact that all details are somewhat magnified through the severity of the symptoms.

TABLE 1.—*Shock Produced in Unanesthetized Dogs by Ascaris Extracts*

| Dog | Weight of Dog, Kg. | Dose of Extract Injected, Cc./Kg. | Symptoms Observed *  |
|-----|--------------------|-----------------------------------|--|
| 53  | 11                 | 1.2                               | 2 to 4 min. later: vomiting, defecation, dyspnea; 6 to 25 min. later: prostration, unconsciousness; 45 min. later: bloody diarrhea continuing until 4 hr. later; recovery  |
| 55  | 11                 | 1.2                               | Half minute later: vomiting; 1 to 4 min. later: urination, prostration, defecation; 20 min. later: agonic agitation; 25 min. later: death. Section: enlargement of the liver, enormous hyperemia of abdominal organs, hemorrhages to the intestinal lumen  |
| 60  | 6                  | 0.5                               | 1 min. later: vomiting; 5 min. later: lateral decubitus, apathy; 7 min. later: prostration, defecation, pupillary dilatation; 8 to 10 min. later: prostration, filiform pulse; 35 min. later: first signs of recovery; 68 min. later: bloody diarrhea; 170 min. later: liquid bloody feces, still prostrated; died overnight                                   |
| 56  | 15                 | 0.8                               | 1 min. later: vomiting; 4 min. later: defecation, dyspnea; 10 min. later: prostration in lateral decubitus; 15 min. later: restlessness; 23 min. later: elimination of urine; 27 min. later: agonic agitation; 32 min. later: death. Section: enormous enlargement of the liver, hyperemia of abdominal organs, mucus and blood in the lumen of the intestines |
| 62  | 8                  | 0.5                               | 2 min. later: defecation, vomiting, urination; 7 min. later: prostration in lateral decubitus; 27 min. later: restlessness; 34 min. later: bloody diarrhea; 1 hr. later: complete recovery   |
| 57  | 13                 | 0.4                               | 3 min. later: dyspnea; 10 min. later: somnolence in lateral decubitus; 25 min. later: somnolence; 1 hr. later: recovery; slight bloody diarrhea  |
| 65  | 7                  | 0.4                               | 3 min. later: urination, defecation; 4 min. later: prostration; 8 min. later: defecation; 30 min. later: total recovery  |

\* Time is indicated in minutes after the injection of the extracts.

*Perfusion of Liver with Total Citrated Blood.*—In 10 dogs we performed the perfusion of the isolated liver with total citrated blood. The amount of citrate used varied from 25 to 20 per cent. It is apparent (table 2) that in all cases there was a definite retention of leukocytes and platelets by the perfused organ. The decrease in the leukocyte and the platelet counts in the perfusates was in most cases sharp enough to be correlated with the injection of the *Ascaris* material into the portal cannula (fig. 1). As a rule, after stoppage of the perfusion, the blood drained from the organ was collected and the leukocytes and platelets counted again. In some cases, especially in those in which there was no appreciable release of active substances, there was considerable increase of leukocytes and platelets in the drainage fluid but the counting was somewhat difficult since the blood elements were agglutinated.

In 1 case (dog 68) the platelets were found in enormous quantity (up to 1,000,000 per cubic millimeter) in the drainage fluid, and the leukocytes increased from a minimum of 1,750, attained at the sixth passage, to 5,650, in the fluid at drainage. In another case (dog 66), the platelets increased from a minimum of 50,000, at the sixth passage, to 161,000, attained after stoppage of the perfusion, and the leukocytes from 750 to 4,900, in the same circumstances. In all those cases, the platelets appeared to form conspicuous aggregates in the Giemsa-stained smears of the drainage fluid. In the case (dog 67) in which there was considerable increase in histamine and heparin in the perfusates fig. 1A), the number of the platelets in the drainage blood remained low (62,000).

Although the histamine was regularly released and found in a free form in the drainage fluid and especially when the liver was excised

TABLE 2.—*Experimental Perfusion of the Liver with Total Citrated Blood; Changes in Histamine and Leukocyte-Platelets After the Injection of Ascaris Extracts*

| Dog | Histamine, Micrograms/1 Cc. |       |          | Leukocytes ( $\times 10^3$ ) |       | Platelets ( $\times 10^3$ ) |       |
|-----|-----------------------------|-------|----------|------------------------------|-------|-----------------------------|-------|
|     | Before                      | After | Drainage | Before                       | After | Before                      | After |
| 48  | 0.02                        | 0.07  | 0.15     | 3.1                          | 0.5   | 523.0                       | 158.0 |
| 65  | 0.03                        | 0.07  | 0.33     | 5.3                          | 1.6   | .....                       | ..... |
| 66  | 0.05                        | 0.10  | 0.12     | 4.7                          | 0.4   | 220.0                       | 47.0  |
| 67  | 0.07                        | 0.61  | 0.16     | 6.0                          | 0.4   | 215.0                       | 60.5  |
| 68  | 0.0                         | 0.02  | 0.13     | 3.0                          | 1.7   | 445.0                       | 186.0 |
| 69  | 0.01                        | 0.03  | 0.06     | 9.6                          | 1.2   | 843.0                       | 390.0 |
| 70  | 0.0                         | 0.05  | 0.15     | 5.1                          | 0.6   | 225.0                       | 23.7  |
| 71  | 0.08                        | 0.06  | 0.26     | 3.1                          | 1.1   | 409.0                       | 29.8  |
| 72  | 0.01                        | 0.05  | 0.12     | 3.4                          | 0.1   | 445.0                       | 80.0  |
| 77  | 0.09                        | 0.16  | 0.22     | 5.9                          | 2.7   | 350.0                       | 78.0  |

with a sharp knife, the amounts liberated were not in most cases so conspicuous as it appears in vivo after the injection of the *Ascaris* extracts into the veins of the intact animal. This might be due to either of the following reasons: (a) the addition of the anticoagulant (sodium citrate) would protect the aggregates of platelets in such a way that their disintegration is only partial; (b) the in vivo conditions are difficult to duplicate in experiments of perfusion. In 1 case (dog 67), however, the discharge of histamine and heparin was especially conspicuous and of the order of magnitude as it occurs in vivo. This definitely proves that intact blood contains all the factors which are necessary to bring forth a discharge of histamine and heparin from liver cells when the antigen is injected.

*Retention and Lysis of Platelets in the Liver of Intact Dogs Receiving the Ascaris Extract.*—The perfusion experiments described have shown that the vessels of the liver might work as a filter for clumped leukocytes and platelets after the injection of the *Ascaris* material into the portal cannula. There was clear indication that platelets

formed aggregates that could be found in the drainage fluid after stoppage of the perfusion. In a few cases, a fragment of the perfused liver was cut with a knife directly into a 3.8 per cent solution of sodium citrate and smears made for microscopic examination. Enormous

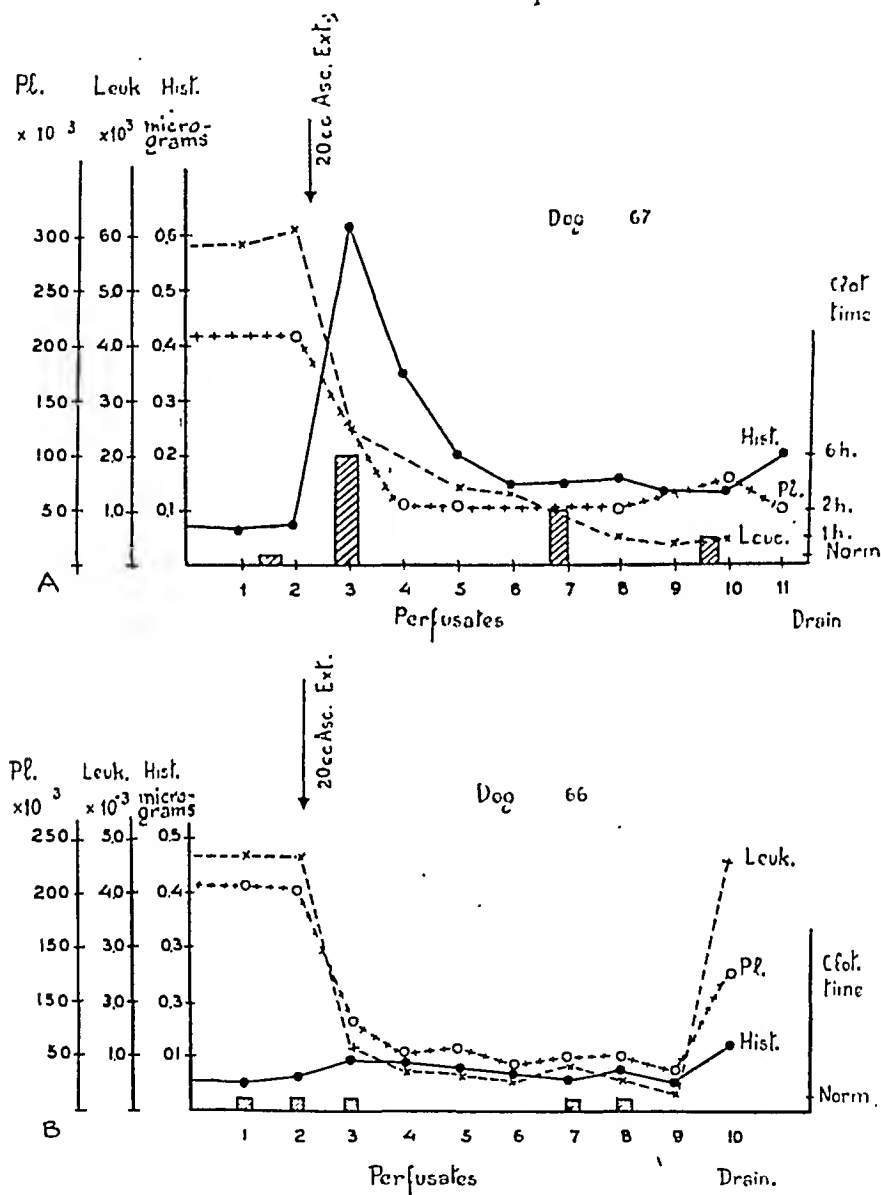


Fig. 1.—Experiments of perfusion of the livers of dogs 66 and 67. In both cases there was a sharp reduction in leukocytes and platelets in the perfusates immediately after the injection of the extract. Note the correlation between the retention of blood elements and the discharge of active substances (dog 67).

aggregates, of 20 or more platelets, were found all over the slide. This fact is an indication that those aggregates were probably protected by the anticoagulant used in the perfusing experiments.

In another series of experiments we have tried to get a proof of a similar retention of platelets by the liver of the intact animal. The animals were anesthetized with morphine plus dial and the blood pressure of the carotid artery recorded. Before the injection the abdomen was opened and a piece of the liver cut directly into a 3.8 per cent solution of sodium citrate. The piece of the liver was rapidly freed of the excess of bloody fluid and carefully rubbed over a microscope slide. By use of the technic described, the platelets were found almost uniformly distributed all over the smears (fig. 2*a*). Besides rare



Fig. 2.—Giemsa-stained smears from pieces of dog liver, before (*a*), immediately after (*b*) and ten minutes after (*c*) the injection of *Ascaris* extract. The animal died in fifteen minutes, showing enormous increases in blood histamine and heparin. The aggregates seen in the second slide are disintegrated and vanishing in the last smears. Note the change of colorability of the platelets in *c*.  $\times 1,077$ .

leukocytes, there were many large endothelial cells, probably originating in the liver capillaries. One to two minutes after the injection of the *Ascaris* material, another fragment of the liver was taken, in absolutely identical circumstances. Since the organ was found enormously swollen by that time, the collecting of a small piece of the organ was rather easily performed. In most of the cases, the smears obtained from this second piece of liver show enormous aggregates of platelets (over 100 platelets clumped in a single mass) scattered over the slide (fig. 2*b*) but mostly around the mentioned endothelial cells. In the most favorable cases, hundreds of those aggregates can be found in a single smear, and if one tries to count the platelets it becomes clear that most of them belong to aggregates and only a few are uniformly distributed among the erythrocytes.

In the smears obtained from the pieces of liver taken many minutes after the shock there was a definite decrease both in the size (fig. 2c) and in the number of the aggregates, this being good evidence that the earlier aggregates have been dissolved during the reaction. We cannot admit that the platelets returned to the general circulation, since the animal died in fifteen minutes, without recovery, and the liver became more and more engorged with blood. Besides that, the counting of platelets in the blood collected in the femoral vein did show a lasting decrease, almost to zero, of those elements. It seems logical to conclude that the aggregates of platelets disintegrated during the shock. This was definitely suggested by the observation of the smears from pieces of liver taken two, five and ten minutes after the injection of the *Ascaris* material. Although the aggregates of platelets had a bright appearance in the first smears, they somewhat changed their colorability in the later stages of the shock, and in the last smears they showed only scarce eosinophil granules at the places where there should have been aggregates of platelets.

*Plasma Trypsin During the Shock.*—Plasma trypsin has been studied in the human being mainly in connection with clinical events. There is no detailed study of the variations of this enzyme under several morbid conditions experimentally induced in animals. As intact blood seems to carry most of the factors which are necessary for the discharge of histamine and heparin from dog liver during anaphylactic shock, it seemed to us advisable to study plasma trypsin during the different phases of the shock in an attempt to verify whether activation of this enzyme might be the final step in the mechanism of discharge of those active substances.

As shown by Schmitz<sup>7</sup> and Iyengar and co-workers,<sup>5</sup> trypsin is found in the plasma in bound and "free" forms. Free trypsin can be estimated after precipitation of plasma with 10 volumes of acetone, while total trypsin is estimated after precipitation of the plasma with 2.5 per cent trichloroacetic acid solution. Although the detailed description of the technic employed and the results already obtained under several experimental conditions will constitute the object of a separate paper, it seems convenient to present here a few typical experiments concerning the problem under study. Table 3 shows the results obtained in experiments on liver perfusion of 6 dogs. It appears clear that, although some increase of free trypsin was consistently observed, there was a definite reduction of it when the samples were collected at the height of the reaction. In the case of the isolated liver of dog 67, in which there was a considerable release of histamine and heparin, this

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7. Schmitz, A.: *Ztschr. f. physiol. Chem.* 250:37, 1937.

was clearly observed in the third perfusate, coinciding with the peak of histamine and heparin. Also the reduction of free trypsin was more apparent in the drainage fluid, in which the amounts of active substances increased. The correlation between this decrease in free trypsin and the appearance of heparin in the perfusates is suggested also by similar observations obtained in the intact dog and also by the fact, which we have verified, that heparin when added to plasma definitely reduces the proteolytic activity of free trypsin and, in a much less extent, of total trypsin. It also became clear that some trypsin is retained by the liver submitted to the perfusion, but in some cases definite increases in total trypsin were observed, not only in perfusion experiments but also in the intact animal, as shown in table 4.

TABLE 3.—*Total and Free Trypsin in the Plasma of Perfusates Taken at Different Stages of the Perfusion\**

| Dog | Perfusates  | Plasma Trypsin<br>(Mg. NPN/100 Cc.) |       | Dog | Perfusates  | Plasma Trypsin<br>(Mg. NPN/100 Cc.) |      |
|-----|-------------|-------------------------------------|-------|-----|-------------|-------------------------------------|------|
|     |             | Total                               | Free  |     |             | Total                               | Free |
| 66  | 1st, before | 74.0                                | 3.5   | 69  | 1st, before | 57.5                                | 1.0  |
|     | 9th, after  | 32.2                                | 8.6   |     | 3d. after   | 64.0                                | 21.0 |
|     | 12th, after | 33.5                                | 30.5  |     | Drainage    | 59.0                                | 0.0  |
| 67  | 1st, before | 97.0                                | 60.0  | 70  | 1st, before | 66.0                                | 24.0 |
|     | 3d, after   | 86.0                                | 1.5   |     | 7th, after  | 71.0                                | 19.5 |
|     | 8th, after  | 99.5                                | 100.0 |     | Drainage    | 71.0                                | 27.0 |
| 68  | 1st, before | 122.0                               | 59.0  | 71  | 1st, before | 72.5                                | 48.7 |
|     | 7th, after  | 214.0                               | 134.0 |     | 7th, after  | 32.0                                | 33.0 |
|     | Drainage    | 168.0                               | 1.5   |     | Drainage    | 32.0                                | 33.0 |

\* All figures indicate the amount of nonprotein nitrogen per hundred cubic centimeters of plasma after an incubation of forty-eight hours, at 38 to 39 C. Before and after refer to the moment of the injection of the ascaris extract into the portal cannula. The dog numbers compare with those given in table 2.

In 8 anesthetized dogs we have estimated total and free trypsin in oxalated plasmas collected at several stages of the shock. It is apparent (table 4) that the same reduction in free trypsin was observed in most of the cases, especially in those in which the shock had been particularly severe, with considerable increases in blood histamine and appearance of anticoagulant in the circulating blood. In those cases, the increases in total trypsin were more steady and in a few cases significant. In the cases of dogs 84, 85 and 86 we have explored the latent period in an attempt to catch the initial changes of trypsin in the samples of blood collected in the portal vein. This procedure was rather to be condemned since the handling of abdominal organs during the start of the shock somewhat reduced the severity and rendered it slower in its development, as verified in separate experiments. But even when blood from the portal vein was collected as soon as one or two minutes after the injection we observed in 2 cases a decrease and only in 1



case (dog 86) a significant increase in free trypsin. In the latter case the shock was exceptionally mild, without increase in histamine in the blood and with slight increase in blood incoagulability.

TABLE 4.—*Estimations of Plasma Trypsin (Total and Free) During the Shock Produced by Ascaris Extracts in Intact Dogs \**

| Dog | Blood Samples         | Plasma Trypsin<br>(Mr. NPN/100 Cr.) |      | Intensity of Shock |
|-----|-----------------------|-------------------------------------|------|--------------------|
|     |                       | Total                               | Free |                    |
| 43  | Before.....           | 72.5                                | .... | +                  |
|     | 13 min. after.....    | 69.5                                | .... |                    |
| 47  | Before.....           | 94.0                                | 43.2 | ++++               |
|     | 12 min. after.....    | 111.5                               | 31.2 |                    |
|     | 18 min. after PV..... | 25.1                                | 14.6 |                    |
| 50  | Before.....           | 94.0                                | 44.0 | ++++               |
|     | 13 min. after.....    | 92.0                                | 4.0  |                    |
|     | 16 min. after PV..... | 89.0                                | 8.0  |                    |
|     | 30 min. after PV..... | 112.0                               | 52.0 |                    |
| 51  | Before.....           | 152.0                               | 87.0 | ++++               |
|     | 8 min. after.....     | 104.0                               | 16.0 |                    |
|     | 13 min. after PV..... | 100.0                               | 15.0 |                    |
|     | 21 min. after.....    | 120.0                               | 12.0 |                    |
| 74  | Before.....           | 128.0                               | 26.0 | ++                 |
|     | 10 min. after.....    | 117.2                               | 31.2 |                    |
|     | 30 min. after.....    | 55.4                                | 3.2  |                    |
| 84  | Before.....           | 136.4                               | 37.0 | ++++               |
|     | 2 min. after PV.....  | 143.4                               | 31.0 |                    |
|     | 4 min. after PV.....  | 162.6                               | 32.6 |                    |
|     | 16 min. after PV..... | 150.3                               | 26.9 |                    |
|     | 18 min. after.....    | 132.2                               | 15.0 |                    |
| 85  | Before.....           | 105.8                               | 28.8 | ++                 |
|     | 1 min. after PV.....  | 85.6                                | 14.4 |                    |
|     | 8 min. after PV.....  | 135.5                               | 26.4 |                    |
|     | 15 min. after PV..... | 137.5                               | 20.8 |                    |
| 86  | Before.....           | 105.0                               | 13.1 | +                  |
|     | 2 min. after PV.....  | 100.0                               | 23.0 |                    |
|     | 12 min. after PV..... | 110.0                               | 16.3 |                    |
|     | 29 min. after.....    | 88.8                                | .... |                    |

\* The samples collected at the trunk of the portal vein are marked PV. The intensities of the shock mean: +, mild shock, with prompt recovery in less than ten minutes; ++, more prolonged fall of the carotid blood pressure, but recovery occurring in more than fifteen to twenty minutes (usually there were small increases in blood histamine and moderate changes in the coagulability of the blood); +++, fatal shock, death occurring by secondary shock, two or three hours later; +++++, death in less than twenty minutes. The figures indicate the increases in nonprotein nitrogen per hundred cubic centimeters of plasma, after an incubation period of forty-eight hours at 38 to 39 C.

#### COMMENT

Considerable work has been done in the past to show the participation of leukocytes and platelets in the genesis of anaphylactic shock,<sup>8</sup> and many persons have attempted to show that a decrease in the white

8. Andrewes, F. W.: *Lancet* 2:8, 1910. Widal, F.; Abrami, P., and Brissaud, E.: *Presse méd.* 28:181, 1920. Webb, R. A.: *J. Path. & Bact.* 27:79, 1924. Achard, C., and Aynaud, M.: *Compt. rend. Soc. de biol.* 67:83, 1909. Kopeloff, N., and Kopeloff, L. M.: *J. Immunol.* 40:471, 1941.

blood elements (hemoclastic shock) would be the most important event in anaphylaxis. The fact that an entirely nontoxic substance, such as liver glycogen, can produce enormous decrease in leukocytes and platelets without shock proves that leukopenia and thrombopenia alone cannot explain the genesis of anaphylactic shock. In the second report of this series, we postulated a connection between the decrease in the platelet and leukocyte counts and the discharge of pharmacologically active substances from dogs' liver, on the basis of the finding that glycogen prevents this discharge when previously injected into the animal. We have also assumed that a mechanical obstruction of liver capillaries with clumped white blood elements might be the initial condition leading to the liver stasis and the discharge of histamine and heparin. In certain cases this mechanical obstruction without much histamine and heparin in the blood appeared to constitute the most important etiologic factor for the production of the shock. In the foregoing paper we adduced proofs for this retention of leukocytes and platelets by the liver, not only in vitro (perfusion experiments) but also in the intact animal. The correlation between the discharge of histamine and heparin and the retention of the leukocytes and the platelets by the isolated liver was also strongly suggested by those experiments. In the intact animal we have observed that the enormous aggregates of platelets which are found in smears of pieces of the liver taken immediately after the drop of blood pressure in the carotid artery disappear or become highly altered six to ten minutes after the shock, this being a clear indication that the aggregates of platelets are lysed or otherwise disintegrated during the shock.

There still is a gap to be filled in this chain of events leading to the discharge of histamine and heparin. As shown before,<sup>9</sup> histamine is promptly released by the interaction of proteolytic enzymes. When one considers the rapidity of the discharge of free histamine by trypsin as verified in perfusion experiments on dog liver or guinea pig lung it seems logical to conclude that the histamine must be linked to the end of the amino acid chains constituting normal cell proteins. The specificity of this linkage is of the arginine-amide or lysine-amide type, as shown before.<sup>10</sup> This linkage can be specifically ruptured by trypsin. On the other hand, we have proofs that trypsin also releases heparin. This was shown by estimating heparin in the blood of intact dogs submitted to trypsin shock<sup>11</sup> and also by direct experiments on perfusion of the liver with crystalline trypsin. Besides histamine, there was a release of an anticoagulant that might be tested in the boiled perfusates,

9. Rocha e Silva, M.: Arch. f. exper. Path. u. Pharmacol. **194**:335, 1940.

10. Rocha e Silva, M., and Andrade, S. O.: J. Biol. Chem. **149**:9, 1943.

11. Rocha e Silva, M., and Dragstedt, C. A.: Proc. Soc. Exper. Biol. & Med. **48**:152, 1941.

therefore after destruction of the trypsin. Since trypsin releases also adeny compounds and a slowly reacting substance, as shown by Trethewie,<sup>12</sup> it remains clear that the type of injury produced by trypsin is of the same kind as that produced by anaphylaxis. This analogy was repeatedly emphasized by us<sup>13</sup> and also by Feldberg<sup>14</sup> and Dragstedt and Wells.<sup>15</sup>

The first question that arises is to know which trypsin is the agent concerned in the reaction. Since intact dogs' blood is necessary for the reaction leading to the release of histamine and heparin one is

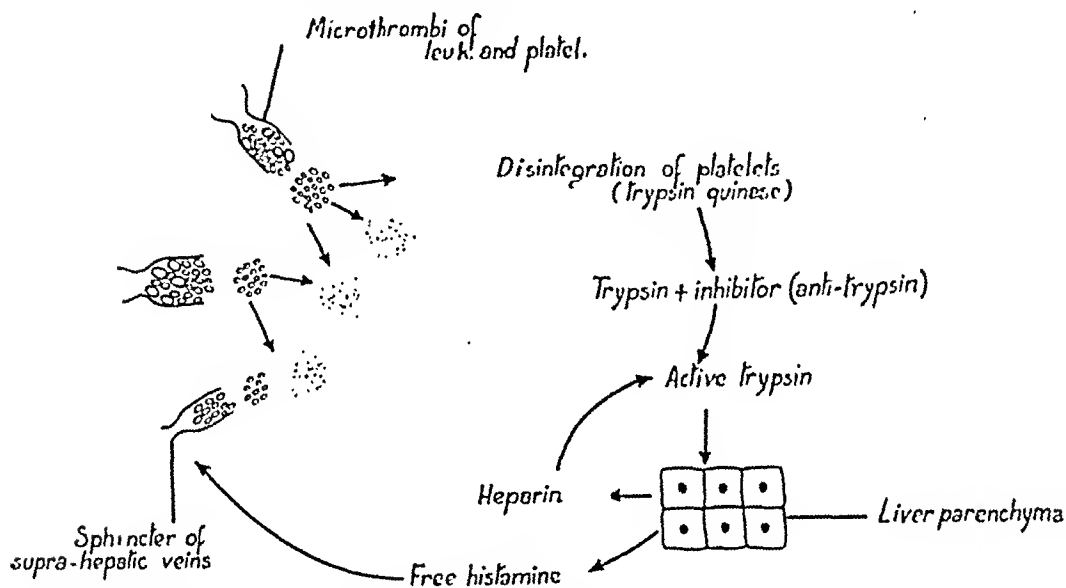


Fig. 3.—Probable chain of reactions leading to the discharge of histamine and heparin from dog liver parenchyma during anaphylactic shock.

bound to take into consideration the possibility of an activation of plasma trypsin as the ultimate mediator for this release from dogs' liver. As shown by Iyengar<sup>16</sup> and confirmed in our laboratory, platelets contain a trypsin quinase which ruptures the combination of trypsin with the inhibitor (antitrypsin). Therefore, if platelets are clumped and lysed in the liver capillaries, it becomes clear that activation of plasma trypsin might be the final step leading to a discharge of histamine and heparin. The scheme of figure 3 was drawn to visualize those probable interrelationships.

12. Trethewie, E. R.: Australian J. Exper. Biol. & M. Sc. **20**:49, 1942.

13. Rocha e Silva, M.: J. Allergy **15**:399, 1944; footnote 9.

14. Feldberg, W., in Luck, J. M.: Annual Review of Physiology, Stanford University, Calif., Annual Reviews, Inc., 1941, vol. 3, p. 671.

15. Dragstedt, C. A., and Wells, J. A.: Quart. Bull. Northwestern Univ. M. School **18**:104, 1944.

16. Iyengar, N. K.: Proc. Indian Acad. Sc., Sect. B **15**:106 and 123, 1942.

The final proof for this theory would be the demonstration that the complex trypsin plus inhibitor is split during the shock. We have made many estimations of free and total trypsin before and after the onset of the shock. At the same time, histamine was estimated in the blood and the discharge of an anticoagulant was roughly verified. In such cases in which the shock was maximal and the discharge of histamine and heparin conspicuous, there was drastic reduction of free trypsin, although total trypsin was unchanged or definitely increased. This diminution of free trypsin at the height of the shock can be attributed to the release of heparin. There is considerable work done to show the antitryptic action of heparin.<sup>17</sup> More recently, Wells and co-workers<sup>18</sup> were unable to demonstrate any antitryptic effect by heparin, using hemoglobin as a substrate. The differences in the substrates used might explain the contradictory results referred to previously. In the case of plasma trypsin, we have found a definite antagonizing effect by heparin when tested on free trypsin. When total plasma trypsin was made free by a precipitation with dilute trichloroacetic acid (2.5 per cent solution) heparin no longer displayed antitryptic action. It seems that the plasma contains a factor that complements the antitryptic effect of heparin. This factor would remain in solution after precipitation of trypsin plus substrate by trichloroacetic acid. Whether this factor can be identified with the heparin complement found by others<sup>19</sup> in the blood is a question requiring further experimentation.

All the facts considered, it seems rather difficult to put into evidence any activation of tryptic agents during anaphylactic shock in the dog. The discharge of histamine and heparin by trypsin is so sudden that there is no way of detecting the enzyme in a free form, since the discharge of heparin will instantaneously blockade its enzymatic activity. This might explain the failure of Dragstedt and Wells<sup>15</sup> and of us to show any increase of free trypsin during anaphylactic shock. Other systems which are being studied in our laboratory might be more successfully used to test the final implications of the theory advanced.

Remaining also obscure is the origin of the extraproteolytic activity appearing in the plasma after the injection of the *Ascaris* extracts, both

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17. Horwitt, M. K.: *Science* **92**:89, 1940. Glazco, A. J., and Ferguson, J. H.: *Proc. Soc. Exper. Biol. & Med.* **45**:43, 1940.

18. Wells, J. A.; Dragstedt, C. A.; Cooper, J. A., and Morris, H. C.: *Proc. Soc. Exper. Biol. & Med.* **58**:57, 1945.

19. Quick, A. J.: *Proc. Soc. Exper. Biol. & Med.* **35**:391, 1936. Ziff, M., and Chargaff, E.: *J. Biol. Chem.* **136**:689, 1940.

in vivo and in vitro (perfusion experiments). Since part of the trypsin might be retained in the organ, it appears probable that the increases would be even more conspicuous than those actually determined. The disintegration of blood elements might provide for some of this extra trypsin, but we must also consider the possibility of a release of proteolytic enzymes from the liver parenchyma itself, as shown by Rawlinson and Kellaway<sup>20</sup> to occur in certain forms of injury to the cells.

#### SUMMARY

Experiments made on the unanesthetized dog have shown the close similarity between the symptoms characterizing the shock produced by *Ascaris* extracts and those which are peculiar to anaphylactic shock. When all the results presented in this and the two preceding papers of this series are summed up, it seems logical to conclude that the two types of shock have the same mechanism.

When the isolated dog liver is perfused with citrated whole blood contained in paraffined receptacles, a conspicuous decrease in leukocytes and platelets follows the injection of *Ascaris* extracts into the cannula. In most of the cases, small amounts of histamine and of an anticoagulant (heparin) are released to the perfusing blood, and in 1 case considerable amounts of both were discharged from the perfused liver. This definitely shows that intact blood contains the factors which are necessary to produce a release of histamine and heparin from liver cells when the extract is added.

In microscopic examinations of smears made from pieces of the liver taken before and after the shock in the intact unanesthetized animal, platelets are found forming enormous aggregates which disappear or partially disintegrate during the later stages of the shock.

Plasma trypsin (free and total) was estimated in the blood used for perfusion of the liver before and after the injection of the *Ascaris* extracts. Similar determinations were made in the circulating blood of the intact animal given *Ascaris* extracts intravenously. Although in a few cases there was a clear indication of an activation of plasma trypsin, in most of the cases, especially when the blood was collected at the height of the shock, there occurred a definite decrease in free trypsin. This diminution in free trypsin was ascribed to the appearance of heparin in the circulating blood.

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20. Rawlinson, W. A., and Kellaway, C. H.: *Australian J. Exper. Biol. & M. Sc.* **22**:69, 1944.

An attempt to understand the mechanism of anaphylactic shock in the dog was made on the basis of the obvious correlation between the discharge of histamine and heparin and the clumping and disintegration of blood elements, especially platelets, occurring inside the liver capillaries.

## REVIEW OF UROLOGIC SURGERY

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### KIDNEY

*Stone*.—Boyd<sup>1</sup> states that in operations for stones in the kidney one of the important duties of the surgeon is prevention of recurrence of stones by removal of all existing causes of formation of stones and by employment of an operative technic in which damage to the renal substance is limited to that which is absolutely necessary. It is necessary for the surgeon to have (1) a knowledge of the normal circulation in the kidney and of the variations which are by no means infrequent and (2) to know the conditions which are generally accepted as being the cause of or predisposing to the formation of stones. Briefly, these can be placed under four headings: (1) precipitation of urinary salts in the calices and pelves, (2) lack of free drainage from the kidney, or so-called urinary stasis, (3) injury to the mucous lining of the calices and pelves and (4) urinary infection with bacteria, which leads to urinary decomposition and damage to the mucosa. Rarely are stones caused by any single factor.

At nephrolithotomy the incision through renal substance should be made at the point where the arterial circulation of the kidney divides. Unobstructed postoperative drainage of urine is often best obtained by a nephrostomy tube, and whenever an infected kidney is opened prolonged drainage of the wound in the abdominal wall by means of rubber tubing will prevent closure of the abdominal wall before the deeper, more cellular parts of the wound have healed and expelled any infection.

1. Boyd, M. L.: *Kidney Operations in Renal Calculus*, South. M. J. **36**: 723-731 (Nov.) 1943.

Hamer and Mertz<sup>2</sup> discuss disappearance of renal calculi following employment of solution G, a solution of citric acid, magnesium oxide and sodium carbonate of  $p_H$  4. The patient was a woman who had alkaline renal calculi which had been present since pyelolithotomy had been performed three years previously. The principal stony mass was removed at a second pyelolithotomy, and several clusters of calculi which were not removed at this operation were dissolved by the persistent use of solution G. Ten months after the patient was dismissed from the hospital renal function was improved and roentgenologic examination revealed no shadow of a stone.

Scholl,<sup>3</sup> in discussing this paper by Hamer and Mertz, states that he was not so fortunate as they in dissolving a stone in 1 case. The patient was a woman 20 years old who had a small stone in a single remaining kidney. Because she had had a difficult time when the right kidney was removed, she refused operation. She had one episode of ureteral obstruction on the left side which was relieved by the pushing of the stone back to the renal pelvis, insertion of a ureteral catheter and injection of solution G by the continuous drip method. The stone could not be seen on roentgenologic examination, and it was thought that the stone had disappeared but three months later, when roentgenologic examination was performed, the stone was observed again. The ureteral catheter was reinserted, and continuous irrigation was carried out for five days, after which the stone again disappeared from the roentgenogram. Four months later, it was reforming. Apparently the matrix of the stone remained, but all the shadow-casting substance was dissolved.

Keyser,<sup>4</sup> in discussing the paper of Hamer and Mertz, states that his interest in the problem goes back to 1932, when he was able to dissolve a recurrent phosphate stone almost completely by urinary acidification by means of an acid diet and by administration of dilute nitrohydrochloric acid by mouth and as an irrigant through indwelling catheters. After this, further well known efforts were made by him and others. The use of acid-ash diets, vitamin A, citrate and buffered citrate solutions, such as solution G, of Suby, was sponsored by their several proponents. Each of these in turn was applied at times, with seeming success. However, on the whole, the use of measures for dissolution

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2. Hamer, H. G., and Mertz, H. O.: Disappearance of Renal Calculi Following the Employment of Solution G: Report of a Case, *Tr. Am. A. Genito-Urin. Surgeons* **37**:115-121, 1944.

3. Scholl, A. J., in discussion on papers of Foulds,<sup>5</sup> Hamer and Mertz,<sup>2</sup> Bugbee, Bumpus and Braasch and Goyanna,<sup>13</sup> *Tr. Am. A. Genito-Urin. Surgeons* **37**:147-148, 1944.

4. Keyser, L. D., in discussion on papers of Foulds,<sup>5</sup> Hamer and Mertz,<sup>2</sup> Bugbee, Bumpus and Braasch and Goyanna,<sup>13</sup> *Tr. Am. A. Genito-Urin. Surgeons* **37**:150-152, 1944.



was disappointing. Hegar several years ago suggested that the softer elements of recurrent concretions are dissolved and that the dense, hard calculi, which stand out so strikingly in roentgenograms, remain most resistant.

In the past three years a study of dissolution of stones *in vitro* has been made by physical chemists at the Virginia Polytechnic Institute. Scherer and Claffey, of this institution, in collaboration with Keyser analyzed several hundred urinary calculi. These were placed in an especially constructed continuous irrigator with thermostatic control. The gamut of solvents was run. They found that solution G (the citrate-magnesium solution of Suby) was probably the best of the solvents. However, its effect was not always striking, especially when oxalate or urate was in preponderance. To a greater degree, the density and crystalline nature of the stone seemed to affect its solubility. Keyser found that preliminary application of enzymes would definitely accelerate the rate of dissolution of these stones when the solvent was applied to them *in vitro*. Of these enzymes, 0.5 per cent solution of urease, if applied for a short time, would increase the disintegration of the stone when it was subjected subsequently to the action of solution G in the irrigator. This was especially true when alkaline earth calculi were used. The action of this enzyme seems to be related to its effect on the colloid framework of the stone. If the calculus was ground to powder and this powder dissolved in solution G, its organic and mineral components would be separated by dialysis. When the organic matter thus separated was treated with a solution of urease at 38 C. for six hours, the mass would swell to five hundred times its original volume. Thus the action of this enzyme, urease, seems to be one of causing a swelling of the organic matter in the stone. This, in consequence, increases the surface action between the crystalline matter of the calculus and the ions of the solvent.

The use of these irrigating solutions as solvents is disappointing when stones are dense. The solutions are useful, however, in dealing with small, softer recurrences, especially in the bladder, where tidal irrigation may be used. In the bladder softer alkaline stones, incrustations on tumors or ulcers and incrustated cystitis may be treated with reasonable hope of success. The work done with urease and other enzymes in the test tube offers hope that better methods of attacking the problem may be devised. As yet it is difficult to apply such treatment without the all too frequent hazard of sharp reactions. Unless the patient tolerates irrigation well and unless after a few days some evidence of dissolution is apparent, it is Keyser's opinion that persistence in such treatment should be avoided.

Foulds<sup>5</sup> reports a case of renal calculi and parathyroid adenoma. Stones had formed in both kidneys in a period of several years when studies of the concentration of calcium and phosphorus in the blood were first made. Though the blood calcium levels were raised significantly, the normal phosphorus level together with the oxalate type of stone and the absence of changes in the bones led Foulds to abandon the diagnosis of hyperparathyroidism. Eight years later, when unmistakable findings were present, such as bilateral renal calculi, pain in the bones, fatigue, weakness, roentgenologic evidence of osteitis fibrosa cystica, elevated levels of blood calcium and decreased levels of blood phosphorus, correct diagnosis was made and proved by operation and pathologic examination of the adenoma, which had been removed.

Keyser,<sup>6</sup> in a discussion of Fould's paper, states that it brings up the interesting relationship between hyperparathyroidism and calculous disease. For some reason hyperparathyroidism does not seem to occur so frequently in the South as in other geographic areas. Keyser has had the opportunity of observing 4 cases in which lithiasis was present. The diagnostic criteria of hyperparathyroidism are not always clearcut. Changes in bones, elevated levels of blood calcium, low levels of blood phosphorus and hyperexcretion of calcium in the urine confirm the diagnosis. In cases in which no changes have occurred in the bones but in which excessive excretion of calcium in the urine, perhaps with low levels of serum phosphorus, low levels of calcium and low levels of serum protein, is found, diagnostic problems arise. Renal insufficiency with retention of calcium may present diagnostic difficulty.

As an example Keyser presents the case of a woman aged 22. Pronounced osteoporosis of the skull, clavicles and long bones was present, and these bones were thinned out almost to paper thickness in certain areas. A huge stone was found in the left ureter, and multiple shadows were observed in the right kidney. A level of calcium of 13 to 15 mg. per hundred cubic centimeters of serum, a level of phosphorus of 2 mg. per hundred cubic centimeters of serum and a urinary excretion of 400 to 500 mg. of calcium on a low calcium diet comprise the typical picture of hyperparathyroid disease. A tumor of the parathyroid, almost the size of a golf ball, was removed. After a stormy postoperative course the patient recovered enough to have the ureteral stone removed. Results of laboratory tests of blood and urine returned to normal limits.

*Tuberculosis.*—In 19 cases of renal tuberculosis reported by Cibert, Gayet and Mafart,<sup>7</sup> there were twenty-six pregnancies, of which twenty

5. Foulds, G. S.: Renal Calculus with Parathyroid Adenoma, Tr. Am. A. Genito-Urin. Surgeons 37:109-113, 1944.

6. Keyser,<sup>4</sup> pp. 149-150.

7. Cibert, J.; Gayet, R., and Mafart, Y.: Tuberculose rénale et grossesse, J. d'urol. 52:62-65 (May-June) 1944.

went to term, three terminated in premature delivery and three in abortion. Deliveries were normal in 2 of 3 cases in which the mothers were suffering from renal tuberculosis; 1 woman had three normal pregnancies after removal of the more involved kidney, although tuberculosis was present in the remaining kidney. Evidence of aggravation of renal tuberculosis during pregnancy was present in only 3 of the cases, but in 7 cases an exacerbation of symptoms followed within a few weeks after delivery. Nephrectomy may sometimes be necessary in the early stage of pregnancy in unilateral renal tuberculosis if severe or moderately severe symptoms are present and especially if cystitis is present. In bilateral renal tuberculosis, when there are urinary symptoms nephrectomy is indicated in early pregnancy if one kidney is involved much more extensively than the other. If both kidneys are much involved and cystitis is severe, therapeutic abortion or premature induction of labor must be considered. The authors were of the opinion that with the modern methods of treatment and care of tuberculous patients cases of severe renal tuberculosis are not encountered so frequently as they formerly were.

In the discussion of this paper, Michon<sup>8</sup> reports 3 cases of unilateral renal tuberculosis in pregnant women; symptoms were mild, and little or no cystitis was present. Pregnancy and delivery were normal, and urinary symptoms were not increased. Nephrectomy has since been performed in 2 of these cases, without complications. In another case of bilateral renal tuberculosis, two normal pregnancies and deliveries occurred; the patient improved definitely under medical treatment, and no evidence of any aggravation of the renal tuberculosis by either pregnancy was found.

Nesbit, Keitzer and Lynn<sup>9</sup> present data on 260 cases of genito-urinary tuberculosis in which the patients have been followed for a period of five years or more. It is pointed out that in this series men are affected more frequently than women, in a ratio of about 2:1, and that the urine in about a third of the cases was infected secondarily by organisms other than the tubercle bacillus. In 50.3 per cent of the cases in which nephrectomy was performed the patients were living an average of eleven years after operation, while in 81.3 per cent of the cases in which operation was not performed the patients died in an average of three years. The authors could not state that an accompanying genital complication in men increases the mortality rate in renal

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8. Michon, L., in discussion on Cibert, Gayet and Mafart,<sup>7</sup> pp. 85-87.

9. Nesbit, R. M.; Keitzer, W. A., and Lynn, J. M.: The Prognosis of Renal Tuberculosis, Treated by Nephrectomy, and the Outlook of the Patient Who Is Considered Unsuitable for Operative Treatment, *J. Urol.* 54:227-234 (Sept.) 1945.

tuberculosis, and they assume that the higher rate among men is due to the higher mortality rate of tuberculosis generally in this group.

Three facts derived from these figures are proved to be statistically significant: 1. In cases in which nephrectomy is performed the survival rate will be lower if acid-fast bacilli are demonstrated (by inoculation of a guinea pig) in the urine from the remaining kidney than it is if the urine from the remaining kidney is normal. 2. In tuberculosis of the urinary tract the period of survival of women is longer than that of men. 3. The mortality rate for genitourinary tuberculosis is adversely influenced by the presence of lesions of the bones, joints or lungs. The operative mortality rate for nephrectomy was 0.88 per cent. The prognosis was bad in tuberculous perinephric abscess; the operative mortality rate was 30 per cent, and 30 per cent of the survivors lived less than one year.

*Hydronephrosis.*—Servelle<sup>10</sup> reports 6 cases of hydronephrosis and megaloureter. Treatment in 2 consisted in removal of the aorticorenal ganglion on the affected side and in 4 in infiltration or resection of the splanchnic nerve. It was found that removal of the ganglion relieved pain but did not reduce the size of the ureter or of the renal pelvis. In 2 cases resection of the splanchnic nerve was performed; in both, results were good, symptoms were entirely relieved and the size of the renal pelvis and of the ureter was definitely diminished. In 1 case in which the renal pelvis was greatly dilated, preliminary infiltration of the splanchnic nerve during operation (nephropexy) caused a sudden contraction of the renal pelvis. Subsequently resection of the splanchnic nerve was performed on the affected side; symptoms were relieved permanently, and hydronephrosis was diminished more than half. One patient who had bilateral hydronephrosis was treated by infiltration of both splanchnic nerves. Symptoms were relieved, and diminution of the hydronephrosis occurred. Section of the splanchnic nerve was advised, but the patient did not return for this operation. In the sixth case, the patient was pregnant and dilatation of the renal pelvis and ureter was discovered when pyelonephritis developed. Lavage of the pelvis and infiltration of the splanchnic nerves resulted in a complete clearing up of the pyelonephritis and pronounced diminution of the size of the ureter and pelvis. Infiltration of the splanchnic nerves is well tolerated in pregnancy.

On the basis of his results, the author concludes that unilateral hydronephrosis and megaloureter are best treated by resection of the splanchnic nerve, which should be combined with removal of the upper part of the lumbar chain. In certain cases, as in pregnancy or diabetes,

10. Servelle, M.: Traitement neuro-chirurgical de l'hydronéphrose et du megauretère, J. d'uroł. 51:57-67 (May-June) 1943.

infiltration of the splanchnic nerve is sufficient. If hydronephrosis and megaloureter are bilateral and equally severe on both sides, bilateral splanchnicectomy and sympathectomy done in stages are indicated, with an interval of two or three weeks between operations. If the lesion is less severe on one side, infiltration of the splanchnic nerve on this side may be sufficient, with splanchnicectomy and sympathectomy on the more severely affected side. If this is not sufficient lumbar sympathectomy may also be performed high on the less severely affected side.

*Tumors.*—Tahara and Hess<sup>11</sup> report two large fatty tumors of the kidney. It is interesting to note that these tumors had existed for a considerable period, that they apparently caused hypertension and loss of weight and that they were both associated with unilateral chronic pyelonephritis. In both cases, nephrectomy reduced blood pressure to within normal limits. Both patients were greatly improved by operation, and both tumors must be considered as benign from the pathologic reports but both had definite malignant characteristics.

*Typhoid Infections.*—Abramson<sup>12</sup> states that typhoid infection of the kidney is probably commoner than it is believed to be and reports a case of primary renal typhoid infection in a 37 year old white man. Calculi and pyelonephrosis were also present, and enteric typhoid was excluded.

The chain of events leading to primary typhoid disease of the kidney is the ingestion of a massive dose of bacilli followed by transient bacteremia and subsequent renal damage and bacilluria. If renal pathologic changes had occurred previously, the danger of continued infection is greater. The persistence of bacilluria depends on the amount and type of renal damage. In the majority of cases renal typhoid is secondary to enteric typhoid and occurs with the acute infection in convalescence or even years later. With continued renal infection it is usual to find some other pathologic entity of the kidney as a contributing factor. The organism usually is carried to the kidney by means of the blood stream, and bilateral renal infection results. The condition may become unilateral when more serious pathologic changes exist in one kidney and the other kidney clears subsequently.

Renal typhoid may be manifested by bacilluria, pyelonephritis, pyelonephrosis or perinephric abscess. Acute pyelonephritis is characterized by cortical suppurative nephritis and may be associated with pyelitis, ureteritis and cystitis. Pyelonephrosis and perinephric abscesses are usually late manifestations of the same disease process. Miliary abscesses may occur in cases in which the condition is acute, and death

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11. Tahara, C., and Hess, E.: Massive Renal Fibrolipoma: Report of Two Cases, *J. Urol.* **54**:107-115 (Aug.) 1945.

12. Abramson, D. J.: Renal Typhoid Fever: Presentation of a Case of the Primary Type, *J. Urol.* **54**:422-429 (Nov.) 1945.

occurs. Pyuria alone is associated simply with toxemia. Treatment in general is the same as for other types of bacillary infections of the kidney. Probably one of the most important single factors in treatment is the removal of the obstruction. By the promotion of adequate drainage, infection will be resolved more readily. Sulfonamide drugs, particularly sulfadiazine, deserve further trial. Pelvic lavage with antiseptics or use of an indwelling ureteral catheter is of value.

*Hypertension and Hypernephrosis.*—Braasch and Goyanna<sup>13</sup> state that nephroptosis per se is seldom, if ever, an etiologic factor in hypertension. In 133 cases of nephroptosis, hypertension was present in 16. In none of these cases was nephroptosis regarded as the etiologic factor. In the majority of cases of nephroptosis the blood pressure is average or less than average. Most of the patients are of the hypotonic type. It would seem that any compression of blood vessels in the renal pedicle which might result from nephroptosis is dissimilar to the pathologic condition in the circulatory system which was involved in the Goldblatt experiment. Urinary retention which may result from nephroptosis does not cause hypertension unless it is accompanied with intrarenal circulatory imbalance, such as sometimes occurs subsequent to secondary urinary infection.

*Obstruction.*—Soley<sup>14</sup> reviews 19 cases of obstruction at the ureteropelvic junction in children. Ten of the patients were boys and 9 were girls. Their ages were from 8 months to 14 years. Fifteen were 10 years of age or less. The right ureter was involved in 7 cases and the left in 7 cases, and bilateral involvement was present in 5. The factors regarded as causing the obstruction were: stenosis in four ureters, aberrant vessel in seven ureters (2 patients with involvement of the right ureter, 3 with involvement of the left and 1 with bilateral involvement), adhesions in four ureters (2 patients with involvement of the left ureter and 1 with bilateral involvement) and double kidney in 2 cases. In the cases of double kidney the upper ureter overlays the lower, obstructing the latter. The following methods of treatment were employed. Six ureters were dilated, and all the patients were considered definitely improved. Nephrectomy was performed in 5 cases. The results were considered to be failures. All 5 patients were treated late in the course of the disease, and 2 presented palpably enlarged kidneys. Foley Y operation was performed in 3 cases. All patients were considered to have improved. In 1 case the aberrant vessel was severed and nephropexy was performed. Postoperative dilation was performed. The result was good. In 1

13. Braasch, W. F., and Goyanna, R.: Hypertension and Its Relation to Nephroptosis, *Tr. Am. A. Genito-Urin. Surgeons* **37**:141-144, 1944.

14. Soley, P. J.: Ureteropelvic Obstructions in Children, *J. Urol.* **55**:46-51 (Jan.) 1946.

case, both ureters were treated only by nephrostomy, use of splinting catheters and severance of adhesions. The result was poor on both sides. In the 2 cases of double kidney, in which the upper ureter blocked the lower, heminephrectomy relieved the lower duct of obstruction and left an important amount of good, functioning tissue. One patient with bilateral involvement refused treatment of any kind.

*Pyelocystostomy.*—Wright<sup>15</sup> reports a case in which pyeloecystostomy was performed, the second operation of its kind so far as he could learn and the first in which only a solitary ectopic, hydronephrotic kidney existed. The patient, a white man aged 42 years, complained of repeated attacks of severe colicky pain in the lower left portion of the abdomen, of five or six months' duration. In the course of the attacks the output of urine was always scanty, and immediately after the attacks, which usually ended suddenly, urine was passed in abundance. Recently he had become conscious of an extremely tender, palpable mass in the lower left portion of the abdomen, which felt to him to be as large as an orange. This diminished in size on the cessation of the attacks of colic but enlarged with the return of the abdominal pains. An intravenous urogram showed that no dye was excreted in one hour from either renal region, and only a faint shadow was seen in the bladder. Cystoscopy revealed that the bladder was normal and both orifices were situated normally. No peristalsis or ejaculations of urine could be seen on either side, and no indigo carmine appeared from either orifice in forty minutes after intravenous injection of the dye. A 5 F. ureteral catheter met an obstruction on the right side, 3 cm. from the orifice, through which the smallest filiform catheter could not pass. On the left side, a 5 F. catheter passed 12 cm. up and tapped urine under strong pressure. Seven fluidounces (210 cc.) of clear urine drained in forty minutes from the catheter in the left ureter. A retrograde pyelogram on the left side revealed an ectopic kidney with a hydronephrotic pelvis. On the right side the ureter apparently ended blindly 3 cm. up from the orifice. At operation the lower border of the renal pelvis was first attached to the lower part of the posterior wall of the bladder by several interrupted sutures of surgical gut, the purpose being to protect the anastomosis to be made from undue tension. An extraperitoneal, suprapubic cystotomy was then made, through which the finger was introduced for guidance. Corresponding vertical incisions, each 3.5 cm. long, were made in the bladder and the renal pelvis, and these were sutured together with surgical gut in the same manner as is employed in gastrojejunostomy. This produced a communication between the cavity of the bladder and the interior of the renal pelvis, through which the index finger could be

15. Wright, B. W.: *Pyelo-Cystostomy in a Solitary Ectopic Kidney*, J. Urol. 54:413-421 (Nov.) 1945.

passed easily, without constriction. Five weeks later, cystoscopy showed the stoma to be open and the edges were firmly healed. Eleven months after operation, it was felt that the patient owed his life to pyelocystostomy.

*Resection.*—Fey<sup>16</sup> distinguishes true partial nephrectomy from the so-called partial nephrectomy, in which one of the two sections of a double kidney with two pedicles and two ureters is removed. In true partial nephrectomy a considerable portion of a single kidney with only one pedicle and one ureter is removed. This involves difficulty in hemostasis and in closure of the corresponding calix. The procedure has been rendered easier and safer by use of the electric knife. In 2 of Fey's cases partial nephrectomy was performed because of renal calculi situated in the lower pole of the kidney. The patients were relieved of symptoms, and the kidney on which operation was performed was functioning at the time of the report. In 1 case partial nephrectomy was carried out because of pyonephrosis involving the lower pole. There was definite improvement after operation, but later total nephrectomy was necessary because a fistula formed in the wound, which had healed previously. Examination of the kidney after removal showed that the origin of the infection was outside the kidney and that the kidney itself was functioning. Therefore, partial nephrectomy had been justified, but this case indicates the need of adequate and prolonged drainage of the perineal space after this operation. In the fourth case partial nephrectomy was done because a clearly defined tuberculous cavity was present and other portions of the kidney were not involved. The patient's condition was greatly improved, but some cystitis persisted, although tubercle bacilli were no longer found in the urine. Nephrectomy was performed, but the patient died four months later as the result of pulmonary abscess. Examination of the kidney after removal showed no active tuberculous lesion; Fey considers that the secondary nephrectomy was not justified in this case.

Ezickson<sup>17</sup> investigated the effect of renal pelvic lavage with a cationic detergent germicide, cetylpyridinium chloride, in a series of 35 cases. The solution was used for one hundred and thirty treatments, and sixty-seven cultures of urine were made and studied. The germicide was used in an aqueous dilution of 1:10,000 or 1:8,000. Of seven classes of organisms involved in infection of the urinary tract, cultures were rendered sterile in 6 cases and no change was observed in 8. When

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16. Fey, B.: Quatre observations de néphrectomies partielles, *J. d'urol.* **52**: 57-61 (May-June) 1944.

17. Ezickson, W. J.: The Effect of Renal Pelvic Lavage with Cetylpyridinium Chloride upon Urinary Tract Infection and Urolithiasis, *J. Urol.* **54**:235-240 (Sept.) 1945.



previous cultures of urine were negative, all subsequent cultures were negative after renal lavage, demonstrating the ability of this germicide to prevent infection. There was no evident alteration in the clinical course of the urolithiasis.

The germicide was used routinely in 260 cases for renal pelvic lavage, ureteral catheterization, cystoscopy, irrigation of the bladder or instillation in the bladder and urethral dilatation or instillation. In no instance were signs or symptoms attributable to infection due to instrumentation. On the other hand, in some of the cases, infection of the bladder and urethra disappeared after its use. In no case was there any evidence of irritation attributable to the germicide. It would seem from this study that cetylpyridinium chloride in a concentration of 1:10,000 or 1:8,000 can be used routinely as an effective germicide for instillation into the urinary tract prior to or accompanying instrumentation. It has also proved effective in the treatment of certain infections of both the upper and the lower parts of the urinary tract.

#### URETER

*Stone.*—When a calculus is situated in the lower part of the ureter within 2 to 6 cm. of the ureteral meatus and is palpable on vaginal examination, Leger and Germain<sup>18</sup> maintain that it is best removed by the vaginal route. This operation has not been used frequently in France, but many cases in which this method was used, with good results, have been reported in the American literature. The authors report 1 case in which this method was employed. Dissection of the ureter is performed behind and to the side of the calculus; when the ureter is freed sufficiently it is brought out through the incision in the vaginal wall, and the stone is removed through an incision in the ureter. After removal of the stone the ureter is sutured with fine surgical gut. While some surgeons have used an indwelling ureteral catheter for twenty-four hours after this operation, others do not consider this necessary. The authors did not use a catheter in the case reported, merely a small drain in the vaginal incision before suturing. The drain was removed in forty-eight hours. No postoperative complications occurred.

Prince<sup>19</sup> states that Foley's lumbar ureterolithotomy should be performed immediately in all cases of calculus in the upper third of the ureter, unless they are of such small size that they give great promise of spontaneous passage within a brief period. This operation is carried out through an incision from 7 to 8 cm. in length without cutting any

18. Leger, L., and Germain, A.: *L'uretérolithotomie par voie vaginale*, J. d'urol. **52**:1-4 (Jan.-Feb.) 1944.

19. Prince, C. L.: *Lumbar Ureterolithotomy: The Foley Operation*, J. Urol. **54**:368-373 (Oct.) 1945.

muscle; the ureter is never freed from its bed, and there is a minimum of retroperitoneal dissection. The operation is of beautiful anatomic design and is quick, bloodless and effective. The average postoperative stay in the hospital has been seven days, as compared with 18.4 days in a series of similar cases in which operation was performed by the usual methods of lumbar ureterolithotomy, both muscle cutting and muscle splitting. The postoperative course is extremely smooth, and morbidity is reduced to a minimum.

Dourmashkin<sup>20</sup> discusses cystoscopic treatment of stones in the ureter in his series of 1,550 cases of stones situated at all levels of the ureter and renal pelvis. Cystoscopic manipulation was carried out in 1,253 cases, and in 1,171 cases (93.5 per cent) the stone was expelled. There were no instances of ruptured ureter or mortality resulting from instrumentation. To form a true index of what may be accomplished by transurethral methods, the cases were divided into two groups: (a) patients having small stones, less than 5 mm. in width (689 cases), and (b) those having large stones, 5 mm. and more in width (564 cases). In group a, the stone was passed in 99.7 per cent of cases and in group b in 85.9 per cent.

The principle of providing ample room for the downward passage of the stone at and below its level was followed in this work. This was achieved by dilation of the lower end of the ureter with metallic bougies and by using rubber bags at the higher levels. Passage of an ordinary catheter was sufficient to induce the expulsion of a small stone in the majority of cases. A number of mechanical factors maintain renal drainage in cases of ureteral stone. For this reason patients were allowed to go about with the stone for considerable lengths of time, without any appreciable renal injury. The majority of patients were ambulatory in the period in which treatment was being given. Indwelling multiple catheters do not provide adequate dilatation in cases of large stones and are likely to produce renal infection.

Forcible extraction of stones in Dourmashkin's opinion is contraindicated, as the same results may be obtained by more conservative methods outlined in the work, without subjecting the ureter to the ever present likelihood of grave injury.

Sauer<sup>21</sup> reports a case of ureterocele complicated by formation of stones within the wall of the cyst, extension of the formation of stones into the juxtavesical part of the diseased ureter and additional calcareous deposits on the outer wall of the ureterocele. In spite of the extensive-

20. Dourmashkin, R. L.: Cystoscopic Treatment of Stones in the Ureter with Special Reference to Large Calculi, Based on the Study of 1,550 Cases, *J. Urol.* 54:245-283 (Sept.) 1945.

21. Sauer, H. R.: Case of Ureterocele with Stone Formation in Ureter, Ureterocele and Bladder, *J. Urol.* 54:158-161 (Aug.) 1945.

ness of the lesions no significant changes had developed in the upper part of the urinary tract. Administration of the stone-dissolving agent solution G by means of continuous drip irrigation of the bladder resulted in complete disappearance of the incrustations. Thus the wall of the cyst was rendered suitable for transurethral coagulation, and delivery of the stones from the ureterocele and ureter was possible.

When a stone in the lower end of the ureter is not visualized by roentgenologic means, Chevassu<sup>22</sup> found that retrograde ureteropyelography can be carried out. Although the ureteral sound cannot be introduced past the obstruction, the opaque medium introduced into the meatus will pass the obstruction. In the case reported, this procedure was carried out on two different occasions, at an interval of four years. The right side was involved in the first attack and the left side in the second attack.

In both instances the lower portion of the ureter was contracted and the ureter was dilated above the contraction. Chevassu attributes the contraction to spasm caused by the presence of the stone. On the first occasion a small stone was passed spontaneously, with complete relief of symptoms. On the second occasion the stone passed after dilation of the ureter. The best method of localization of a calculus in the lower end of the ureter is by rectal palpation in men and vaginal palpation in women. In women who are thin bimanual examination may be employed, and the calculus may be palpated between the fingers of the hand on the abdomen and the finger within the vagina. In some cases it may be possible to manipulate the stone out of the ureter by this procedure.

*Carcinoma.*—Lazarus and Marks<sup>23</sup> review the literature on primary carcinoma of the ureter and report a case. In 1934, Lazarus collected 68 cases, including 3 of his own. Since then 115 additional cases have been reported. This increased number of cases indicates greater alertness on the part of urologists to the possibility of this disease rather than to an actual increase in incidence. Of the total number of tumors, 42 per cent were of the nonpapillary type. Malignant neoplasms of the ureter were situated in the lower segment of the ureter in approximately 50 per cent of the reported cases and were associated with ectasia of the renal pelvis in 46.4 per cent and of the ureter in 43.7 per cent, due to a tendency for these tumors to occlude the lumen of the ureter. The greatest prevalence of this disease occurred in the sixth and seventh decades. Ureteral carcinomas have pronounced invasive and metastasizing tendencies, par-

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22. Chevassu, M.: Les calculs de l'extrémité inférieure de l'uretère invisibles aux rayons X, *J. d'urol.* 52:39-41 (March-April) 1944.

23. Lazarus, J. A., and Marks, M. S.: Primary Carcinoma of Ureter, with Special Reference to Hydronephrosis, *J. Urol.* 54:140-157 (Aug.) 1945.

ticularly to the regional lymph nodes (28.9 per cent), liver (14.9 per cent) and bones (12.8 per cent).

Although pain, hematuria and the presence of an enlarged kidney are supposed to constitute the characteristic triad of symptoms of this disease, Lazarus found that hematuria alone was by far the outstanding symptom, having occurred in 70.5 per cent of the collected cases. The diagnosis of ureteral tumor cannot be made from symptoms or physical signs, but it can be made from carefully executed and correctly interpreted cystoscopic and roentgenologic findings. Although the presence of a tumor at a ureteral meatus is an extremely suggestive finding, it was noted in only 25.1 per cent of cases reviewed in this series. A clearcut and persistent filling defect, visible in the ureterogram, especially when associated with ectasia of the segment of ureter directly above such a defect, constitutes the only pathognomonic sign of ureteral tumor. Unfortunately, however, because of technical difficulties or of failure to obtain carefully made ureterograms, such defects were demonstrated in only 21.8 per cent of the collected cases.

The chances of demonstrating filling defects in ureterograms would be enhanced if repeated attempts were made to obtain good ureterograms in all cases in which (1) an obstruction is present in the ureter, (2) bleeding occurs through the ureteral catheter as a result of manipulation at the site of the obstruction and (3) no calculus is found at the site of obstruction. Failure to recognize the presence of this disease has led urologists to remove hydronephrotic kidneys only to learn later that hematuria had recurred, thereby necessitating a second operation, for removal of the tumor-bearing segment of ureter. Owing to the difficulty at times of palpating a tumor within the ureter at exploration of the upper part of the urinary tract for hematuria, it seems a better policy to remove the entire ureter along with the kidney, especially when the cause for the bleeding is not found in the kidney. This is particularly true in cases of hydronephrosis or pyonephrosis in which the cause of the pelvic ectasia is not clearly discernible. The procedure of choice in the treatment of this disease is complete extraperitoneal nephroureterectomy. It is recommended that a cuff of vesical wall surrounding the ureteral meatus be included in the operative procedure in cases in which the tumor is situated low down in the ureter, especially when the ureteral meatus is involved.

A careful review of the literature showed the dangers of incomplete urologic examinations for so-called minor urologic complaints. This is clearly demonstrated in the history presented in 1 of the cases reported by Lazarus and Marks, in which the patient was treated perfunctorily for fifteen years for cystitis without being subjected to a thorough urologic examination. The authors feel certain that this lesion would

never have progressed to such large proportions had ureteral catheters been passed during one of the episodes of so-called cystitis.

Bowie and Bors<sup>24</sup> report a case of primary papillary carcinoma of the ureter complicated by severe infection, which made diagnosis more difficult. The operative technic is reported in detail because in this particular case certain well recognized general surgical principles of attacking malignant tumors were employed. The peritoneal cavity was opened to search for evidence of spread of tumor. Dissection was begun in healthy tissue above the tumor, and, after the tumor was reached from above, dissection with an electrosurgical knife was begun on the side of the bladder and the whole tumor removed en masse.

*Ureteral Transplantation.*—Davalos<sup>25</sup> reports a new technic of transplanting both ureters to the rectosigmoid at one operation, together with a report of its experimental employment in 10 dogs. In this operation the ureters are transplanted to the anterior aspect of the rectosigmoid, in the median line (the areas covered by mesenteric circulation being avoided), and a 4 cm. transverse incision in the bowel is utilized. The method differs fundamentally from all previously reported technics.

The operation has the following advantages: 1. The main blood supply of the intestine comes from the mesentery and transversely surrounds the intestine; therefore, a transverse cut in the intestine causes much less damage to the blood supply than does a longitudinal incision, and the bleeding is minimal. 2. Only one operation is required to transplant both ureters in the same incision; consequently the operative work, trauma and chances of leakage are reduced 50 per cent. 3. With this transverse incision it is possible to form a large mucosal flap which acts as a valve and protects the anastomosis against retrograde infection. This flap is formed by the action of the mattress sutures, which, when tied, shorten the intestine on its transverse aspect. 4. The drainage of the ureters is under direct observation of the surgeon during the entire procedure. If the ureters are draining satisfactorily before the mattress sutures are tied, there is no danger of their compression after the sutures are tied.

It is concluded from this study that this new method of transplanting both ureters at the same time is safe and effective. The results in animals have been excellent. In no instance did hydronephrosis follow these experimental operations, one of which was performed one year before the report.

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24. Bowie, C. F., and Bors, E.: Primary Carcinoma of the Ureter, *J. Urol.* **54**:434-437 (Nov.) 1945.

25. Davalos, A.: New Technique of Simultaneous Bilateral Uretero-Intestinal Anastomosis: Report of Experimental Study, *J. Urol.* **54**:357-367 (Oct.) 1945.

## PROSTATE

*Transurethral Operation.*—Greene and Thompson<sup>26</sup> state that introduction of the transurethral method of prostatic operation has removed one of the chief contraindications to prostatic surgical treatment, namely, advanced renal insufficiency. Transurethral prostatic resection can be performed safely on patients suffering from advanced renal insufficiency, and these patients are no longer obliged to lead a life with an indwelling catheter. The important features of management are: (a) improvement or restoration of the acid-base metabolism by the intravenous administration of suitable fluids and the treatment of anemia by blood transfusions; (b) maintenance of a urinary output of 2,000 to 3,000 cc. daily, thereby producing a fall in the nitrogenous waste products present in the blood; (c) drainage by urethral catheter for as short a period as possible (suprapubic cystotomy, with its attendant mortality rate, is not necessary); (d) operation at the first indication that the value for blood urea is no longer falling but has become stabilized, and (e) completion of the resection in forty-five minutes. The period of pre-operative and postoperative hospitalization for patients suffering from advanced renal insufficiency is comparatively short when they are treated by transurethral prostatic resection. Longevity following prostatic resection among patients of this group warrants the procedure. Gastrointestinal symptoms due to renal insufficiency have all been relieved in spite of the fact that renal function remains impaired.

Emmett and his associates<sup>27</sup> state that more than 94 per cent of transurethral prostatic operations performed at the Mayo Clinic were completed in one stage. More than 3.8 per cent of the patients were 80 years of age or older, and the average age for the entire group was 66 years. The average postoperative hospitalization was eight and a half days. Only 7.6 per cent of patients were confined to the hospital for two weeks or more after operation, while only 2.1 per cent were confined for three weeks or more. Eighty-two per cent of the patients were operated on without preliminary drainage. The remaining 18 per cent were prepared by urethral catheterization except for 7 patients (less than 1 per cent) who had suprapubic drainage before resection. The operative mortality rate was 1.3 per cent. In the past few years interest has been increased in transurethral resection of the vesical neck for urinary retention caused by injuries or diseases of the spinal cord. Interest in this subject has increased greatly throughout the country because of the large number of injuries to the spinal cord received in combat by members of the armed forces.

26. Greene, L. F., and Thompson, G. J.: Transurethral Prostatic Resection in Patients with Advanced Renal Insufficiency *J. Urol.* 54:166-173 (Aug.) 1945.

27. Emmett, J. L.; Cook, E. N.; Pool, T. L., and Greene, L. F.: Transurethral Surgery in 1944, *Proc. Staff Meet., Mayo Clin.* 20:469-472 (Nov. 28) 1945.

One hundred and seventy-one patients who had carcinoma of the prostate gland underwent transurethral resection at the Mayo Clinic in 1944. Bilateral orchectomy was performed in 17 of these cases and in 4 other cases in which no prostatic operation was performed. In 1944, bilateral orchectomy was advised only when metastasis was present and giving rise to symptoms.

One of the most important procedures in transurethral operation is transurethral manipulation of ureteral calculi. In the order of frequency with which they are used, the Johnson, Council and Howard spiral extractors are the three stone extractors employed in this work. Only stones in the lower third of the ureter are considered suitable for manipulation. Manipulation of ureteral calculi is an exceedingly difficult technical procedure and should be so considered if a high percentage of successful results is to be obtained and if serious trauma of the ureter is to be avoided. The most important rule is that the manipulation must be done with extreme gentleness. A catheter or extractor should never be forced past the stone. If the instrument cannot be passed with gentle manipulation, some other means should be resorted to for removal of the calculus. Forceful manipulation may result in perforation of the ureter, and after this is done it is usually extremely difficult or impossible to pass a catheter up the ureter for drainage. It is apparent, then, that sufficient room in the ureter in the region of the stone is necessary for successful manipulation. At times a 4 or 5 F. catheter can be passed beyond the stone, yet there is insufficient room for an extractor to pass. In such a case, if the catheter is left in place for from twenty-four to forty-eight hours, enough dilatation may be obtained for passage of the extractor. If the stone is impacted in the intramural portion of the ureter, the roof of the ureter may be excised with a Collings knife through a McCarthy panendoscope, the indwelling ureteral catheter being used as a guide. In this manner the stone may be exposed and flipped into the bladder, or the extractor may then be passed to engage the calculus. When one resorts to such a procedure, it is always wise to have a catheter in the ureter as a guide as after the first cut with the Collings knife it may be difficult to discern the true channel of the ureter.

One of the most disturbing complications that may harass the surgeon in transurethral manipulation of a stone is that he may engage a large stone in the extractor but be unable to pull it through the intramural portion of the ureter or ureteral meatus. One simple satisfactory maneuver may be used in this situation. The cystoscope is removed and the extractor left in place, with the stem of the extractor passing out through the urethra. An 18 F. catheter is passed alongside the stem of the extractor into the bladder and left in for drainage.

The extractor is left in place for from twenty-four to forty-eight hours. At the end of this time the patient is returned to the operating room and is anesthetized. The catheter is removed, and the cystoscope is introduced into the bladder. The stem of the extractor is threaded through the cystoscope. It is usually rather simple at this stage to extract the stone, as the wire basket on the extractor has produced considerable dilatation and only a moderate amount of traction is necessary to complete the procedure.

Emmett and his colleagues are convinced that suprapubic cystotomy for the removal of vesical calculi is only rarely necessary. It is unusual to encounter a stone so large that it cannot be crushed with the Bigelow type of lithotrite. In 1944, litholapaxy was carried out successfully in 56 cases at the clinic. Only 2 patients underwent suprapubic removal of stones. In almost all the cases litholapaxy and transurethral resection were carried out as a one stage procedure. Usually litholapaxy is done first. In an occasional case, however, intravesical tissue may make litholapaxy impossible, so that at least part of the prostatic resection must be done first. Most patients experience no more postoperative reaction from combined litholapaxy and transurethral resection than from transurethral resection alone.

*Carcinoma.*—Darget<sup>28</sup> reports treatment of carcinoma of the prostate with radium, using different methods of application. In 1 case in which prostatectomy had been performed previously, a urethral sound containing two tubes of 10 mg. of radium each was left in situ for three days; the patient was in good health three years later. In 2 cases treatment consisted in implantation of radium needles by both the transvesical and the perineal route. One of the patients was living and well seven years after treatment and the other two years after treatment. In 2 cases, transurethral resection was combined with implantation of radium needles by the perineal route. Both of these patients were living, without signs of recurrence, two years after treatment. Two other patients were treated by perineal implantation of radium alone; these patients were both living and well, 1 nearly six years and the other nearly four years after treatment.

Darget considers that in the initial stage of carcinoma of the prostate the best results are obtained by the implantation of radium by the transvesical and the perineal route simultaneously. If considerable residual urine is present, transurethral resection combined with implantation of radium by the perineal route is indicated, provided that the tumor is not too large. If no residual urine is present and the tumor is relatively small, perineal implantation of radium alone is indi-

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28. Darget, R.: Le traitement actuel du cancer prostatique, *J. d'urof.* 52: 29-32 (March-April) 1944.



cated. In cases in which infection is present or in those in which there is danger of uremia, preliminary cystostomy is indicated and it should be followed by transurethral resection and radium therapy. In cases in which cure appears impossible and the growth is in an advanced stage, transurethral resection relieves the urinary obstruction and is the best palliative measure. For both transvesical and perineal implantation, needles of 3 mg. of radium each are employed; by the transvesical route, these needles are placed 15 mm. apart and by the perineal route 1 cm. apart. For perineal implantation, four to eight needles are used, depending on the size of the tumor. Cystostomy is necessary before transvesical implantation. For perineal implantation alone, an indwelling catheter is employed during the time that the radium implants are in place and for several days thereafter. It has been found that treatment with radium by the perineal route is well tolerated.

In discussing the paper by Nesbit and his associates, Dean<sup>29</sup> states that they established a group treated by castration and, as nearly as possible, a comparative group treated with 1 mg. of diethyl stilbestrol daily. The immediate effects of castration appear to be more spectacular than those of diethyl stilbestrol in the doses mentioned. Whereas the pain from metastasis to bone often disappears within twenty-four to forty-eight hours after operation, relief with the drug frequently is noted only after a week or more.

Dean observed a greater softening and shrinking of the primary tumor after administration of diethyl stilbestrol than after castration. Sixty per cent of Dean's patients relapsed in seven to eight months. He found little difference in the duration of improvement before relapse occurred, whether treatment was with diethyl stilbestrol or castration. The patients who received diethyl stilbestrol and did not relapse at the usual time survived longer and with less evidence of persistence of the primary tumor than did those who underwent orchectomy. After relapse occurs, irrespective of the type of treatment first given, Dean has found little benefit in further treatment. The castrating of patients treated with diethylstilbestrol has not helped, and the treatment of castrated patients with the drug has been equally unavailing. Nor has there been any noteworthy quantitative improvement after the dose of diethylstilbestrol has been increased. In general, patients have improved in proportion to the degree of feminization they show. The men with shrunken external genitalia, enlarged breasts with pigmented nipples and areolas and added weight about the hips have shown greater regression in prostatic carcinoma than have the patients in whom these changes were less pronounced or absent. Dean questions the ability of the most

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29. Dean, A. L., in discussion on papers of Huggins and McDonald, Rathbun and Nesbit and others, *Tr. Am. A. Genito-Urin. Surgons* 37:232-235, 1944.

experienced urologist to be correct invariably if examination is limited to rectal palpation. None of his patients were treated unless the diagnosis was verified microscopically. Dean makes aspiration biopsies, which he has accepted as being accurate because of the extraordinary experience of the pathologist with whom he works. It is a rare prostatic carcinoma which can be positively recognized by rectal touch before it becomes inoperable. Then even the most radical operation cannot be carried out.

#### BLADDER

*Carcinoma.*—Graves and Thomson,<sup>30</sup> in discussing total cystectomy for carcinoma, state that this operation should be performed with the intent to cure and under conditions which render cure possible. It should not be selected, in their opinion, as a method of palliation when the tumor has obviously spread beyond the limits of the vesical wall. They have performed this operation in 28 cases and state the belief that cystectomy is a sound and highly valuable procedure and that in the future it will be employed oftener and with increasingly satisfactory results. The first of the 28 patients was operated on in September 1933. Thirteen of the group are living and free from malignant disease as determined at the time of the last report. The length of the time of survival after cystectomy varied from one month to ten and a half years. Of the last 20 patients, encountered after 1939, 11 patients were living and had no apparent evidence of recurrent carcinoma at the time of their report.

The indications for cystectomy have become definite and clearcut. First, there should be reasonable assurance, based on every possible form of investigation, including abdominal exploration, that no distant metastases are present and that removal of the bladder and its adjacent structures will remove the tumor of the bladder completely. Further, it must be decided that age and general condition will permit the patient to survive the operation and live to enjoy its benefits. As far as age is concerned, Graves and Thomson have adopted a tentative upper limit of 60 years for this procedure and in older patients have hesitated to advise cystectomy. The choice of cystectomy as far as the disease within the bladder is concerned depends on the extent and manner of growth and location of the tumor more than on the result of biopsy. Multiple tumors, often of low grade malignancy, call for cystectomy when they involve so much of the vesical mucosa that local resection is impracticable and destruction by electrocoagulation and radium will virtually destroy the bladder itself. High voltage roentgen therapy should not be relied on in most instances as a method of cure. Its use may be attended by actual disadvantage, moreover, when operation becomes necessary later. This

30. Graves, R. C., and Thomson, R. S.: Total Cystectomy for Carcinoma, Tr. Am. A. Genito-Urin. Surgeons 37:73-82, 1944.

is particularly true of ureterointestinal anastomosis which may be affected adversely by roentgen therapy, probably through the fibrosis which it produces in the walls of the bowel and ureter.

Extensive infiltrating carcinoma, still confined to the bladder, also presents an indication for cystectomy, since radium and roentgen rays usually do not cure tumors of this type and local excision is equally ineffective in most cases. Tumors of the outlet of the bladder, particularly those which overlie the prostate in men, give still another reason for cystectomy, because electrocoagulation and irradiation sufficient to destroy the growth in this region will seriously impair the usefulness of the bladder through occlusion of the urethra and destruction of sphincteric function. Tumors of the bladder contiguous to the prostate are not controlled by radium or any other method of treatment short of complete surgical extirpation of the structures involved.

Finally, tumors of the trigone demand cystectomy when they occlude both ureters or when they encroach on the ureters so closely that their ultimate occlusion, as a result of disease or local treatment, is inevitable. The successful end results of operation for malignant disease of the bladder will depend on the preservation of adequate renal function as well as on the cure of the lesion. Pronounced occlusion of the ureters, one or both, should be regarded to be of serious prognostic significance, since periureteral invasion leads readily to the invasion of lymphatics beyond the limits of the bladder itself.

The final evaluation with reference to the choice of treatment is made at the time of cystoscopic and rectal examinations with the patients under spinal anesthesia. The authors regard this routine use of anesthesia as the most helpful preoperative step that they have taken in the study of these patients. The patient is relaxed and comfortable; the surgeon is not hurried, and the filling and emptying bladder may be watched at leisure. The nature, location and extent of the tumor may be determined better in these circumstances than in any other way. More of the bladder is brought into view, and the relations of the neoplasm to the ureteral orifices and the vesical outlet are much more accurately defined. Most important information with reference to the possibility of cystectomy is obtained finally by rectal examination with the patient under anesthesia. One learns in this way the true size of the tumor if it is palpable, the degree of infiltration through the wall of the bladder, the movability of the mass and its distance of separation from the rectum and the lateral wall of the pelvis.

Graves and Thomson use spinal anesthesia induced by the continuous method of administration, and they have found this technic to be invaluable in these cases. The necessity for a large amount of anesthetic given in one initial dose is avoided; the hazards of shock are greatly

lessened, and patients emerge from prolonged procedures in highly satisfactory condition. The authors also give a description of their method of cystectomy.

Smith,<sup>31</sup> in discussing Graves's article, states the belief that total cystectomy is going to be performed more and more frequently. Smith expresses the opinion that total cystectomy is not a particularly dangerous procedure, as he has performed cystectomy in 10 cases of carcinoma, with only one death. One woman died of coronary disease (proved at necropsy) ten days after the second operation. Her case was unusually successful from the point of view of the operation, as there were no metastases and both kidneys were functioning well.

Jewett<sup>32</sup> gives an analysis of 107 cases of infiltrating carcinoma of the bladder in which necropsy was performed at the Johns Hopkins Hospital. Four important facts were revealed: First, the potential curability varies inversely with the degree of penetration of the wall of the bladder. Second, while the tumor is still confined to the submucosa or muscularis a latent period exists, in which the potential curability is relatively high. Third, complete penetration of the muscularis is associated with low potential curability. Fourth, complete penetration usually causes stony hard induration. This induration in more than 80 per cent of the cases can be recognized by rectoabdominal palpation with the patient under anesthesia, but when doubt exists the induration can be detected readily at laparotomy, at which time the regional lymph nodes and liver also can be examined.

Deming and Linds kog<sup>33</sup> report a case of papillomatosis of the bladder and the urethra. Involvement of the whole urethra by metastases, late metastasis to the right lung and successful surgical treatment of both, the former by excision of the penile urethra and the latter by a pneumonectomy, make the report unique. Although the primary lesion had been fully under control for thirteen years metastasis to the right ilium had developed at the time of this report, and other osseous metastases will probably develop. The histologic classification of papillomas of the bladder gives no opportunity for optimism toward its inherent metastatic quality. The justification of eradication of a solitary distant metastatic lesion is supported on the basis of relief of symptoms and prolongation of life.

31. Smith, G. G., in discussion on papers of Deming and Linds kog,<sup>33</sup> Jewett,<sup>32</sup> Scholl and Graves and Thomson,<sup>30</sup> *Tr. Am. A. Genito-Urin. Surgeons* **37**:83-84, 1944.

32. Jewett, H. J.: *Infiltrating Carcinoma of the Bladder*, *Tr. Am. A. Genito-Urin. Surgeons* **37**:51-65, 1944.

33. Deming, C. L., and Linds kog, G. E.: *Papillomatosis of Bladder and Entire Urethra; Infiltrating Cancer of Bladder; Late Pulmonary Metastasis; Successful Pneumonectomy*, *Tr. Am. A. Genito-Urin. Surgeons* **37**:39-50, 1944.

*Reflux.*—In tuberculosis of the urinary tract involving the bladder, reflux of urine from the infected bladder may occur. Bouchard<sup>34</sup> states that the reflux is due to the destruction of the normal mechanism of the ureteral meatus by the tuberculous lesion in combination with excessive urination and tenesmus of the bladder, which occur in tuberculosis of the urinary tract. Another important factor is the involvement of the vesical neck; inflammatory lesions, even superficial, of the mucosa cause spasmodic contracture of the sphincter. This is not the only cause for failure of normal function of the vesical neck and sphincter. Inflammatory lesions may involve the musculature and especially the interstitial connective tissue, resulting in fibrosis. In renal tuberculosis, the reflux of urine not only affects the infected kidney, but also endangers the opposite kidney. After removal of the affected kidney, if the cystitis persists, reflux of urine may involve the remaining kidney or it may create a fistula in the lumbar wound with discharge of urine through the fistula.

Bouchard reports 5 cases in which such a fistula occurred in the lumbar wound after removal of a tuberculous kidney. He reports 3 cases in which cystography showed reflux to the uninvolved kidney in cases of unilateral renal tuberculosis and 3 cases in which reflux to the remaining kidney occurred after nephrectomy. In cases in which the cystitis cannot be cured by the use of an indwelling catheter and irrigations with antiseptic solutions, especially methylthionine chloride, Bouchard recommends endoscopic resection of the vesical neck, which he considers the best surgical treatment for the relief of urinary reflux.

*Traumatic Paralysis.*—Campbell<sup>35</sup> states that 1 in approximately 30 infants is stillborn and that in about 30 per cent death results from trauma at birth. In 11 to 35 per cent of the group in which death results from trauma, the central nervous system is injured, chiefly by tentorial tears, compression, contusion, crushing or laceration of the brain or spinal cord or of both. Hemorrhage into or about these structures is the striking observation at necropsy. Literature on obstetrics offers no data regarding the incidence of birth trauma as it affects urinary control; yet, by analogy, since injury of the central nervous system in adults commonly produces pronounced disturbances of vesical function, so it must in the newborn. These disturbances usually pass unrecognized at the time but, if the infant survives, may present serious clinical problems in succeeding months. Attention has been called to the late effect of birth paralysis, but apparently it has not been suggested that when

34. Bouchard, R.: Le reflux dans la tuberculose rénale, *J. d'uro.* **51**:133-146 (Nov.-Dec.) 1943.

35. Campbell, M. F.: Traumatic Cord Bladder in a Premature Infant: Successful Treatment by Indwelling Catheterization, *Tr. Am. A. Genito-Urin. Surgeons* **37**:17-19, 1944.

infants have traumatic neurovesical disease the same fundamentals of urologic treatment be observed that apply when the patient is an adult.

Campbell reports a case of injury of the central nervous system at birth which was complicated by traumatic spinal cord bladder in a prematurely newly born infant. The patient was a girl who had been born one month prematurely. A few hours after birth she became cyanotic, yet cried vigorously. Later the child was listless, respirations were shallow and irregular, icterus, grade 1 plus, was noted and subconjunctival hemorrhages in the left eye were observed. A soft doughy mass extending from the pubic region to the umbilicus was detected but disappeared on catheterization. Catheterization and dilation of the urethra to 12 or 15 F. was also recommended, since at that time Campbell thought that retention was probably due to a congenitally tight urethra. It was not until the next day that the neurologic nature of retention was demonstrated. On this day the condition was decidedly worse, respirations were shallow, with an occasional gasp, and dark red blood clots were present in the pharynx. The persistent distention of the bladder was relieved by drainage by an indwelling catheter, which remained in place for one week. Scattered leukocytes were found in the urine, and on culture a mixed infection of colon bacillus and *Staphylococcus aureus* was found. The day after the institution of indwelling catheterization it was noted that the child was definitely improved, respirations were regular and she opened her eyes and responded to stimuli. Relief of pressure of the spinal fluid by spinal tap may also have been a beneficial factor. It was believed by all who saw this patient that the employment of the indwelling catheter at the critical period of vesical retention saved her life.

#### VARICOCELE

Campbell<sup>36</sup> stated that practically all varicoceles in young boys may be classified etiologically as symptomatic, that is, they result from interference with the spermatic venous return, usually by extravascular compression. The last is often the late result of renal trauma and the extensive changes in the perirenal tissue which so commonly follow. The discovery of varicocele in a prepuberal male calls for thorough urologic examination and removal of the etiologic mechanical factor rather than for varicocelectomy. In 1 of Campbell's cases, the patient was a boy 13 months old. A large varicocele on the left side promptly disappeared after nephrectomy for Wilms's tumor. In this instance the tumor was recognized before the varicocele. In contrast, in another case, that of a boy 13 years old who was referred for varicocelectomy, investi-

36. Campbell, M. F.: Varicocele Due to Anomalous Renal Vessel: An Instance in a Thirteen-Year-Old Boy, *Tr. Am. A. Genito-Urin. Surgeons* **37**:13-14, 1944.

gation prompted by the presence of the varicocele revealed asymptomatic hydronephrosis secondary to ureteral compression by an aberrant lower polar renal artery. This artery also compressed the upper part of the left spermatic vein. Treatment in the last-mentioned case consisted in division of the obstructing renal artery and, doubtless unnecessary, similar division of the spermatic vein at the upper end of the large retroperitoneal varicocele. The swelling in this case extended from the testicle to the point of compression of the spermatic vein by the anomalous renal vessel. Three months after operation scrotal palpation disclosed no varicocele, but hydronephrosis due to periureteral scarring existed three years later.

#### URINARY CALCULI

In one year of urologic investigation and practice in a hospital that supplies medical care to the southern part of Ecuador, in 60,000 patients Davalos<sup>37</sup> did not find a single stone in the urinary tract. In the wet tropics the high temperature induces profuse perspiration which, by eliminating a considerable part of the metabolic output through the skin, materially decreases the strain on the kidneys. The low urinary  $p_H$  prevents the growth of urea-splitting organisms (*Proteus vulgaris*, *Proteus ammoniac*, *Escherichia coli* and others), and phosphates and carbonates do not precipitate in the urinary tract. It would appear that, in tropical Ecuador at least, climatic conditions are primarily responsible for the rarity of urinary lithiasis, since the poorly balanced vitamin-deficient diet of the inhabitants far from preventing the formation of stones is conducive to it.

Vermooten<sup>38</sup> states that renal calculi are rare in South African Negroes. He checked 1,000,000 cases of Negroes to a hospital and found only 1 Negro who had renal calculi. The climatic conditions in South Africa are different from those of Ecuador. Although the coastal belt is hot and moist, the climate as a whole is dry and of the desert type, with hot days, cold nights and a short rainy season.

As Davalos has pointed out, in certain areas in the United States calculi are common and in others they are relatively rare. This indicates that other factors are also at work, especially when such episodes as the "stone wave" which swept over Europe, especially Germany, after the first World War are considered. His observations on dietary habits and the acidity of the urine are especially important. He expressed the opinion that these played a considerable part in the absence of calculi in South African Negroes for their diet also tends to have an acid-ash base. The water supply as well as the diet may be of great significance. The diet of the South African Negroes is poor in calcium. Their normal

37. Davalos, A.: The Rarity of Stones in the Urinary Tract in the Wet Tropics, *J. Urol.* **54**:182-184 (Aug.) 1945.

38. Vermooten, V., in discussion on Davalos,<sup>37</sup> p. 185.

daily intake of calcium is much less than that which most textbooks on dietetics indicate to be the normal daily minimal requirement; yet they have a magnificent bony structure and excellent teeth, with few caries. Renal calculi are found in American Negroes though to a less extent than in the white persons. This brings up the point that some racial characteristic may be present. This was emphasized in the observations in South Africa, in which it was found that "Cape-colored" persons (half caste race of mixed Negro and Caucasian blood) had almost as many calculi as Caucasians.

Keyser<sup>39</sup> discusses some of the evidences of the origin of urinary calculi from the physicochemical, bacteriologic and pathologic standpoints as revealed by experimentation on animals and study of stone-forming kidneys. He presented the concept of stone-forming pyelonephritis, which parallels in some degree that of other types of crystalline deposition in tissue. Stone dissolution was discussed from the standpoint of the chemist and of the clinician. It has been and will be further developed.

#### MULTIPLE TUMORS

Hayward<sup>40</sup> reports a case of four primary malignant tumors in a man who was 82 years of age at the time of the report. In order of appearance in a period of two years, they were: (1) basal cell carcinoma, (2) epidermoid carcinoma, (3) adenocarcinoma of the prostate and (4) embryonal carcinoma of a testis. Hayward comments briefly on the literature. He states that Warren and Gates were able to find only 3 cases of three or more primary malignant lesions. Bugher reported 3 cases of three primary malignant lesions. From these reports it must be recognized that the presence of three or four primary malignant lesions is extremely rare and makes this case worthy of reporting. Another unusual feature of the case is the occurrence of an embryonal carcinoma of the testis in a patient of advanced age.

Lombard and Warren, in a recent publication, offer the following conclusions: "There is a greater susceptibility to cancer in persons having one cancer than in the normal population. Whether this susceptibility is caused by the first cancer or is inherent in the individual is not known. There is no evidence to assume that the presence of a skin cancer inhibits other cancers. If anything, the evidence points to the contrary."

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39. Keyser, L. D.: Studies in Urinary Calculosis, *J. Urol.* **54**:194-210 (Aug.) 1945.

40. Hayward, W. G.: Multiple Primary Tumors, *J. Urol.* **54**:307-311 (Sept.) 1945.



## SCHISTOSOMIASIS

The recognition by Peters, Huntress and Porter<sup>41</sup> of 2 cases of bilharziasis, the first in Maine to be added to the literature, increases to 37 the reported proved cases in the United States and Canada and brings this condition to the attention of the urologist at an opportune time. Geographically the distribution of the disease is governed by the existence of a suitable snail host necessary for each of the three types of schistosomes which infect the human body. The finding of the ova in the urine or at biopsy is necessary for a positive diagnosis, but suspicion of the existence of the condition from the history of the case, the symptomatology and the blood picture is grounds for specific treatment.

Man is usually infected by the schistosomes in the water when his skin becomes penetrated by the free-swimming cercariae, whose larvae subsequently migrate into the blood vessels. They are carried to the heart and capillaries of the lungs and are said to reach the liver and remain in the portal system, where they develop and mature. The time required for their ovulation varies with the different species from twenty-seven to sixty days. The site of egg laying depends on the habits of the particular species of worm. *Schistosoma haematobium* deposits its ova particularly in the vesical wall, and *Schistosoma mansoni* and *Schistosoma japonicum* usually in the venules of the intestine and rectum. The developmental cycle outside the human body consists of hatching of the ova in water and the liberation then of a free swimming miracidium resembling a paramecium. The miracidium is attracted to certain species of snails. In the incubation period a local cutaneous reaction consisting in petechial hemorrhages with an inflammatory reaction usually occurs at the point where the cercariae have penetrated. Several days later an urticarial rash may develop, with accompanying pronounced eosinophilia. After the ova have passed from the venules of the vesical plexus into the vesical wall, a pronounced degree of congestion of the mucous membrane occurs and is followed by necrosis and erosion. In the healing process the vesical wall becomes thickened due to the fibroblastic reaction, and crystalline deposits may form about the ova in the wall and mucous membrane.

Terminal hematuria is the outstanding sign of the disease. However, as this is common to many infections, great care in interrogation should bring out the fact that the patient has visited or resided in areas in which the infection is known to be present. Further inquiry may give a definite history of mild dermal involvement during or shortly following his sojourn, or the patient may even state that he has been in poor health, with recurrent attacks of mild fever and general malaise. Bleeding may be accompanied with irritation of the bladder or may be entirely

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41. Peters, C. N.; Huntress, R. L., and Porter, J. E.: Urinary Schistosomiasis: Report of Two Cases in Maine, *J. Urol.* 54:301-306 (Sept.) 1945.

painless, and in some periods the urine may be free from gross blood. Changes in the trigonal mucous membrane from the so-called velvety appearance to granulomatous involvement, even progressing to papillary growth and carcinomatous tumefaction, have been noted.

Antimony in the compound named fuadin has practically displaced all previous treatment. It is given intramuscularly or intravenously daily, and it is recommended that daily doses be increased. The dose starts at 1 cc. and is increased according to tolerance. The dose is leveled to 5 cc. every second day until 40 cc. has been given. Rarely a second course is necessary.

Two cases are reported in detail. In 1 case both *Schistosoma haematobium* and *Schistosoma mansoni* were found.

#### CHYLURIA

Yamauchi<sup>42</sup> reports the clinical, laboratory and statistical study of cases of chyluria. His report is based on the analysis of the records of 45 cases of chyluria which are carefully compared and correlated with those recorded in the literature.

Patients suffering from chyluria had all been exposed to *Filaria* in their lifetime, but filariae were never demonstrated in blood, urine or, in some cases, tissues. The long period elapsing from the last possible exposure to *Filaria* to the onset of chyluria in many of these cases, the absence of eosinophilia in the majority and several other factors indicate that filariasis probably predisposes to this condition but does not actually initiate it. This role, however, is real and definite, and any one who has been exposed to this nematode becomes a potential candidate for chyluria any time, even many years after the exposure.

Urinary stasis has been considered as the exciting cause of chyluria. Rupture of the fornix caused by urinary stasis results in a lymphatico-urinary communication, and chyle appears in the voided urine if the ruptured lymphatic vessels already contain chyle. Except in a few instances minimal pathologic changes sufficient to form varices are probably present in the lymphatics without definite obstruction to the large retroperitoneal lymphatic vessels and thoracic duct. Pregnancy, endocervicitis and prostatic hypertrophy, so frequently found with this condition, become logical concomitant occurrences instead of bizarre associations when viewed in this light.

Chyluria is characterized by the appearance of chyle per se in the voided urine. The presence of fat granules in a colloidal state, the presence of albumin, erythrocytes and lymphocytes, the pyelographic injection of the renal and perirenal lymphatics frequently associated with

42. Yamauchi, S.: Chyluria: Clinical, Laboratory and Statistical Study of Forty-Five Personal Cases Observed in Hawaii, *J. Urol.* 54:318-347 (Sept.) 1945.

rupture of the fornix and pyelovenous reflux and the control of the condition by repeated intrapelvic lavage with sclerosing solutions support the surmise that a lymphaticourinary fistula is present at the fornix of the calices.

The control of chyluria can be accomplished without much difficulty by repeated intrapelvic lavage with solutions of silver nitrate through inlaid catheters, but the cause of urinary stasis must be removed and fat in the diet must be limited after such lavages. The success of such management depends on the extent to which the predisposing and exciting causes can be eliminated.

#### DENGUE

Weyrauch and Glass,<sup>43</sup> in a study of 141 male patients recovering from dengue fever, found that in 8 cases (5.7 per cent) conclusive signs or history of involvement of the urogenital tract was present. Five patients suffered from dengue orchitis, and subsequent atrophy of the testis developed in 3 of these cases. Five patients experienced repeated bloody seminal emissions in the first few months of convalescence. In 2 cases, the latter finding was confirmed by laboratory examination of the spermatic fluid. It was noted that atrophy of the testis sometimes occurred following minimal swelling of the testis. This observation casts doubt on the common assumption that atrophy is caused by compression of the testis incident to tremendous engorgement within its inelastic capsule. Our studies indicate that an active pathologic process may persist in the urogenital tract for several months after the acute febrile phase of dengue fever, as evidenced by hemospermia and progressive atrophy of the testis.

#### REITER'S DISEASE

Colby<sup>44</sup> reviews 3 cases in which the essential features of the syndrome known as Reiter's disease were present. All 3 patients were young men. The typical triad of urethritis, conjunctivitis and arthritis was present. There is insufficient evidence that the disease is contracted by sexual exposure. Bacteriologic studies have failed to identify the causative agent. The course of the disease is unaffected by any known treatment, including penicillin. Instances of permanent articular disability are rare, although a few have been reported. Recurrent ocular, articular and urinary symptoms may occur. Renal complications may occur and be of considerable severity.

43. Weyrauch, H. M., and Glass, H.: Urogenital Complications of Dengue Fever, *J. Urol.* **55**:90-93 (Jan.) 1946.

44. Colby, F. H.: Renal Complications of Reiter's Disease, *Tr. Am. A. Genito-Urin. Surgeons* **37**:93-98, 1944.

## HERMAPHRODITISM

McKenna and Kiefer<sup>45</sup> present 2 cases of true hermaphroditism. One child, 13 years old, had an ovotestis in the scrotum on the right side and an ovary in the inguinal canal on the left. A rudimentary vagina opened into the urethra and pronounced hypospadias was present. The second child, 3 years old, had a testis in the scrotum on the right side and an ovary on the left side of the abdomen, with a tube on the left side and a rudimentary vagina opening into the urethra. Hypospadias was also present. The second case is one of true lateral hermaphroditism, the first nearly so except for a small nodule of ovarian tissue attached to the testis. In each case the ovary was removed, and the testis was the only sex gland remaining.

## OSTEITIS PUBIS

Cohen<sup>46</sup> presents 2 cases of osteitis pubis following suprapubic prostatectomy. Symptoms of osteitis pubis may develop as late as three months after operation, particularly when the condition is associated with delayed operative complications. Treatment with penicillin and sulfonamide drugs did not appear to have any effect on the course of the disease. The clinical progress of osteitis pubis in the majority of instances would appear to indicate an aseptic process of the variety of Sudeck's atrophy, rather than osteomyelitis of the pubis. Roentgenologic findings and absence of response to treatment with the sulfonamide compounds and penicillin tend to confirm this. Orthopedic measures, such as traction or immobilization by a plaster of paris spica cast, usually will give gratifying relief of the pelvic pain.

Muschat<sup>47</sup> reports 2 cases of osteitis pubis following prostatectomy. He states that this condition occurs after operations on the urinary bladder and especially after prostatectomy. The disease begins about ten days after operation but may not begin until two months later. The pain usually starts over the symphysis, gradually shifting to the right or the left of the suprapubic area. Next the pain travels to the crotch, to the triangle of Scarpa and to the inner side of the thighs. Later in the disease there may be pain in the perineum and over the tuberosities of the ischii. The patient experiences excruciating pain in the inner side of the thighs in the form of spasmodic contractions of the adductor muscles. Recovery is slow and tedious, and improvement can be noted only after periods of weeks.

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45. McKenna, C. M., and Kiefer, J. H.: Two Cases of True Hermaphroditism, *Tr. Am. A. Genito-Urin. Surgeons* **37**:21-26, 1944.

46. Cohen, H. H.: Osteitis Pubis, *J. Urol.* **55**:84-89 (Jan.) 1946.

47. Muschat, M.: Osteitis Pubis Following Prostatectomy, *J. Urol.* **54**:447-458 (Nov.) 1945.

The diagnosis is established by roentgenologic examination. Early in the disease no changes are seen. As the disease progresses (about the third week) the roentgenogram reveals some changes in the symphysis pubis; namely, fraying of the periosteum, with a moth-eaten appearance of the symphysis and the ramus pubis on either side. Later, more involvement of bone is seen. Decealeification involves the rami and the inner portions of the ischii until the tuberosities are reached. After eight to ten weeks, recalcification begins, with rapid reconstruction of the structure of the bone. The symphysis, however, remains separated and later becomes completely ankylosed by bone. The bacteria found varies in every case, but the predominant offenders appear to be *Bacillus proteus*, *Esch. coli* and hemolytic and nonhemolytic *Staph. aureus*. The clinical picture is clearcut and the roentgenologic evidence so definite that no difficulty should be encountered in making the correct diagnosis.

Muschat states that this disease is self limited and does not require surgical intervention. If an abscess does develop it should be drained properly. He used 4,000,000 units of penicillin in 1 case, without any subjective improvement. Sulfonamide drugs were administered and did not influence the condition. One thing must be borne in mind, that any manipulative procedure to hasten recovery is strongly contraindicated. It only aggravates the condition and stirs up local trauma, thus actually spreading the disease process and delaying recovery. The ultimate outcome in all these cases is good. The disease does not spread to other structures or organs. The only complication encountered is occasional formation of abscess with restitution after drainage. The only scar demonstrable is complete ossification and ankylosis of the symphysis. This fortunately remains symptomless.

#### ANURIA

Lattimer<sup>48</sup> discusses a plan for management of anuria. He analyzes the various methods of treatment which were used in his series of cases, and the most successful plan of action was selected from this experience. This regimen was followed in the management of his 7 most recent cases of anuria. All 7 patients have recovered. First and foremost, a warning sign was posted on the bed that the total intake of fluid was to be restricted to 1,000 to 1,300 cc. per twenty-four hours according to the patient's size and the temperature of the room. The degree of hydration, concentration of the serum proteins and the blood count were evaluated by determination of the hematocrit level, the specific gravity of the blood and the number of erythrocytes. Any abnormalities were corrected

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48. Lattimer, J. K.: A Plan for the Management of Anuria, *J. Urol.* 54: 312-317 (Sept.) 1945.

to normal levels by infusions of isotonic solution of sodium chloride or transfusions of blood or plasma as indicated by the studies of the blood.

Thorough alkalization of the blood and urine was started at once, especially if there was reason to believe that anuria was due to sulfonamide drugs, transfusion reaction or toxins from traumatized tissues. An infusion of 1,000 cc. of 1.2 per cent solution of sodium bicarbonate in distilled water was started, and 4 Gm. of bicarbonate was given in water every three hours, by mouth and by rectum, until the carbon dioxide-combining power of the blood was elevated to levels of 70 to 90 volumes per hundred cubic centimeters. Whatever urine was then produced was usually alkaline. The  $p_H$  of every urine specimen was determined. A plain roentgenogram of the urinary tract was taken to exclude obstructing calculi from the diagnosis. Cystoscopy with the passage of small ureteral catheters and pyelography with one of the isotonic iodide solutions were advised for most anuric patients. In cases in which sulfonamide crystals were suspected, these examinations were made at once and the ureters and pelvis lavaged for twenty minutes with warm 10 per cent solution of sodium bicarbonate. In other cases it was done at any time within the first two days in order to exclude the diagnosis of structural abnormality. In infants, cystoscopy was deferred as long as possible because of the usual need for general anesthesia. If mechanical obstruction was found, it was corrected at once by operation. Electrolyte levels were watched carefully. If the level of potassium in the serum rose to toxic levels, concentrated solution of sodium chloride or sodium bicarbonate was given. If the level of chlorides in the plasma dropped, sodium chloride was given in adequate doses, usually of 10 Gm. daily. If the sodium chloride was not tolerated by mouth or rectum, it was given intravenously. A high carbohydrate diet which contained a small proportion of protein was given. One or more doses of 50 per cent solution of dextrose were tried arbitrarily in the first two days of anuria. If renal function was not reestablished by these measures, a period of about fourteen days elapsed before further treatment was given if the patient's condition remained good. If anuria persisted after fourteen days of conservative treatment, bilateral renal decapsulation was considered. If cerebral or renal edema was already present, manifested by convulsions or decline in the patient's general condition, an earlier attempt at renal decapsulation might well be indicated. In the period of anuria, the greatest danger was from edema. Pulmonary edema and pleural effusions were complicated by bronchopneumonia, cerebral edema caused convulsions and renal edema led to further renal damage.

Hoffman and Colby<sup>49</sup> review the world literature on cases of incarceration of the penis and add a case, bringing the total number of reports to 114. The various motives involved and the types of constricting bands used are enumerated. An instrument for removing metal rings from the penis is described. The advisability of attempting repair by primary intention in the presence of adequate antisepsis is discussed and favored, and the role of lymphatic location in the satisfactory restoration of structure and function of the organ is suggested. The importance of psychologically intelligent handling of the patient for preservation of effective integrity is stressed.

#### ANTISEPTICS

Menville and Ross<sup>50</sup> stated that the response of gonorrhea to sulfonamide drugs is poor. Gonorrhea treated by the administration of urea in doses of 20, 40 and 60 Gm. daily in conjunction with the administration of sulfonamide drugs responds somewhat better than to sulfonamide drugs alone. The response to sulfonamide drugs with and without urea is greatest in cases in which no previous treatment has been given. The majority of the patients respond to the first course of treatment. The administration of urea in doses of 20, 40 and 60 Gm. daily apparently does not enhance treatment with sulfonamide drugs in cases of sulfonamide-resistant gonorrhea. Urea and sulfonamide compounds are in no way comparable to penicillin in the treatment of gonorrhea. The administration of urea in doses of 20, 40 and 60 Gm. daily does not appreciably elevate the concentration of urea in the urine. Doses of 20 Gm. of urea daily did not appreciably change the level of sulfonamide drugs in the blood in the small series of patients examined.

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49. Hoffman, H. A., and Colby, F. H.: Incarceration of the Penis, *J. Urol.* 54:391-399 (Oct.) 1945.

50. Menville, J. G., and Ross, C. W.: Urea and Sulfonamides in the Treatment of Gonorrhea, *J. Urol.* 54:211-219 (Aug.) 1945.

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## **PATHOLOGIC INTERVERTEBRAL DISK AND ITS CONSEQUENCES**

**A Contribution to the Cause and Treatment of Chronic Pain Low in the Back  
and to the Subject of Herniating Intervertebral Disk**

**OLAN R. HYNDMAN, M.D.**

**DENVER**

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### **I. INTRODUCTION**

Some time ago I studied with Dr. Arthur Steindler, of Iowa City, the problem of chronic pain low in the back in relation to the syndrome of herniating intervertebral disk. We made an attempt to differentiate what we called true herniating, or ruptured, disk from pain low in the back with "reflex" pain. Two observations were outstanding. First, a patient without herniation of the intervertebral disk seldom complained of pain below the knee, although he frequently complained of pain down the thigh to the knee. Second, as Steindler pointed out, it was possible to find points of maximum tenderness about the sacrum and gluteal regions in such a patient which if made anesthetic with procaine hydrochloride would completely relieve the patient of his discomfort temporarily. A patient with a herniating, or ruptured, disk causing compression of a nerve root would definitely not experience relief



of sciatic pain by such an injection of procaine hydrochloride and for obvious reasons, viz., the source of the pain in the nerve root was untouched by the procaine hydrochloride. Hence, Steindler introduced his test with procaine hydrochloride as a means of differentiation between chronic pain low in the back with, perhaps, "reflex" pain down the thigh and herniating disk with "radiating" pain down the sciatic distribution. The term "reflex" is used to imply that the referred pain is not due to compression of a nerve root, while "radiating" implies that it is due to compression of the nerve root. The results of these studies were published by Steindler and Luck,<sup>1</sup> Steindler<sup>2</sup> and Hyndman, Steindler and Wolkin.<sup>3</sup> At that time we were content with recognizing that a patient with chronic pain low in the back and perhaps reflex pain who was temporarily relieved by the injections of procaine hydrochloride (positive results in the test with procaine hydrochloride) did not have a herniating disk and therefore was not a candidate for operation. In such a case we made a diagnosis of "myofascial syndrome," which implies a strain or sprain of the ligaments and of the tendinomuscular structures about the lumbosacral and sacropelvic regions. This would be cause for the pain low in the back and the reflex pain in the thigh that may accompany it. Such patients were segregated from those who presented definite syndromes of herniating disk, and they were put through the ritual of conservative treatment, including rest in bed, with traction to one or both lower extremities, belts,<sup>4</sup> corsets, braces and, as the court of last appeal, tibial bone grafts<sup>5</sup> in an attempt to stabilize the lumbosacral joint.

*Definition.*—It is appropriate at this point to define degenerating and herniating disks, so that references to the two entities throughout the paper might be clearly understood. A degenerating intervertebral disk is one in which the nucleus pulposus and the annulus fibrosus are undergoing disintegration. While the gross pathologic changes of a degener-

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1. Steindler, A., and Luck, J. V.: Differential Diagnosis of Pain Low in the Back; Allocation of Source of Pain by Procaine Hydrochloride Method, *J. A. M. A.* **110**:106-113 (Jan. 8) 1938.

2. Steindler, A.: The Interpretation of Sciatic Radiation and the Syndrome of Low Back Pain, *J. Bone & Joint Surg.* **22**:28-34 (Jan.) 1940.

3. Hyndman, O. R.; Steindler, A., and Wolkin, J.: Herniated Intervertebral Disk: A Study of the Iodized Oil Column; the Procaine Test in Differential Diagnosis from Reflected Sciatic Pain, *J. A. M. A.* **121**:390-401 (Feb. 6) 1943.

4. The narrow so-called sacroiliac belt can hardly be more than psychologic therapy in the treatment of the symptoms for which it is prescribed. If any attempt is made by external appliance partially to even stabilize the lumbosacral joint, a tall corset with rigid stays or, better, a steel spring back brace is required. Many corsets are efficacious only in the support of a protruding abdomen.

5. The usual bone graft is too short. Some of them do not "take" and, hence, serve no purpose at all. In order to obtain a successful "take," or fusion, the patient should be immobilized in a body cast for at least eight weeks or more. On the whole, the results of bone grafting have been unsatisfactory.

ating disk are obvious to inspection, the cause and nature of the pathologic changes are not yet so clearly understood. Herniation is only an advanced stage of degeneration, but when the term "degenerating" is used it is implied that there is as yet no bulge, or herniation, that would cause pinching or compression of an adjacent nerve root. The term "degenerating" rather than "degenerated" is used because the process, however slow, is probably continuous and progressive.

Herniating disk is the term used to designate a disk that, because of weakened capsule or annulus, bulges, partly or entirely, into the spinal canal beyond physiologic limits. The bulge, or herniation, compresses a nerve root against the adjacent ligamentum flavum, giving rise to symptoms and signs appropriate to compression of the nerve root. The annulus may rupture and the nucleus extrude through it. In the interests of specialized and descriptive nomenclature such types should be specified, but for all practical purposes these types, which are discussed under terminology, may be encompassed in the broader term, "herniating" disk. Here again the term "herniating" is preferred to "herniated," in order to imply a continuous process. When a part or all of the nucleus pulposus is completely sequestered and extruded, the process may have likely reached an end stage and, in this case, could be more properly termed herniated disk. In any case, when the term herniating disk is used throughout this paper, it is intended that it be synonymous in connotation with various terms that have appeared in the literature, viz., protruded disk, slipped disk, ruptured disk or fractured disk.

Throughout this presentation considerations relating to the degenerating and the herniating disk must run concomitantly, because the two are only different aspects of the same pathologic process and the symptom complexes they provoke are closely associated and often combined. The consideration of the two as being different entities is justified only because of the fact that they do provoke distinctly different syndromes, namely, chronic pain low in the back and pain from compression of a root. Since the common location of pathologic changes in disks is being considered, the fourth and fifth lumbar disks, the pain from compression of the roots specifically resolves itself into the well known sciatica or radiating pain in the sciatic distribution. Criticism may be proffered for separation of this pathologic change in disks into two distinct entities from a pathologic standpoint, but the separation is justified because each is associated with its own characteristic syndrome. The two syndromes may exist each to the exclusion of the other, or they may be combined.

## II. CAUSE OF CHRONIC PAIN LOW IN THE BACK

A number of facts and thoughts presented themselves which led to the conclusion that most chronic pains low in the back are due to soft or degenerating intervertebral disks.

1. Seventy-five per cent of the patients in my experience who have proved herniating, or ruptured, disks give histories of chronic pain low in the back for some time before they experienced sciatic radiation or the symptoms and signs of compression of a nerve root. Some patients do indeed give histories of sudden and spontaneous onset of sciatic pain due to compression of a root and deny absolutely the preexistence of pain low in the back. At operation, most of these patients present laterally placed herniations of only small portions of the nucleus pulposus. The small sequestered portion is seated in a definite small pocket, which, when cleanly and thoroughly curetted out, proves to have a hard, firm and glistening wall. The remainder of the disk is not soft but has a normal firmness and integrity. I feel that this finding is significant when correlated with the absence of chronic pain low in the back in the history. Such patients present the syndrome of only compression of a root from the beginning. The operative relief of pain is immediate and the results most satisfactory because the syndrome is not complicated by the effects of a totally degenerating disk—effects which are outlined further in this paper.

Three of the patients in my total experience who gave histories of chronic pain low in the back preceding the onset of sciatic radiation stated that the pain low in the back disappeared in time after the sciatic radiation developed. Although only a conjecture, this might indicate that after the nucleus was spontaneously extruded a firm fixation between the adjacent vertebrae could be established by the development of a fibrocartilaginous scar, thus remedying the cause of the pain low in the back. Nature, in this respect, attains the result that the surgeon seeks by removal of the pathologic nucleus. The extruded nucleus, however, provokes a new type of pain for the patient—that due to compression of a nerve root. Compression of a nerve root alone does not cause the type of chronic pain low in the back under discussion. This is attested to by the patients who have sciatic radiation without ever having experienced pain low in the back.<sup>6</sup> Chronic pain low in the back and sciatic radiation (or pain in a nerve root) are distinctly separate clinical entities and have entirely different explanations, although the two are attributable to different aspects of the same pathologic process.

2. A study of the pathologic and histologic changes of the intervertebral disks below the fourth and fifth lumbar disks, and sometimes both, in a patient with the type of chronic pain low in the back under consideration is convincing and is elaborated under the section devoted to pathology.

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6. In cases of benign tumor (i. e., perineural fibroblastoma) involving a root or roots of the cauda equina, the patient will experience radiating pain in a distribution corresponding to the involved roots, but pain low in the back of the type discussed in this paper is not a feature of the syndrome.

3. If the disk below the fourth or fifth lumbar spaces is soft and degenerating there will be an instability of the lumbar or the lumbosacral joint—an instability that orthopedists must have recognized years ago and which they sought to remedy by bone graft. Such an instability occasions an undue stress and strain on the perispinal ligaments and muscles and is the probable cause for the "myofascial syndrome," or pain low in the back. Although much effort has been made to demonstrate nerve fibers in the disk, I do not believe that the disk itself is the source of pain, or else, in keeping with this thesis, Steindler's test with procaine hydrochloride would never give positive results. Jung and Brunschwig,<sup>7</sup> after careful study, found no evidence of nerve fibers in the intervertebral disks. They found nerve fibers only in the anterior and lateral longitudinal ligaments. Keyes and Compere<sup>8</sup> remarked that, therefore, trauma or disease affecting the intervertebral disks can produce subjective symptoms only in proportion to the degree in which the adjacent structures are involved. Steindler's observations on the test with procaine hydrochloride provide a capital contribution to the problem of pain low in the back because they throw light on its true nature and lead one to the primary cause.

I should not presume to imply that a degenerating disk is the *sine qua non* for every case of strain or sprain low in the back. The object of this paper is to propose that a degenerating disk is the one commonest primary cause for the type of chronic pain low in the back to be described.

### III: SYNDROME OF CHRONIC PAIN LOW IN THE BACK DUE TO DEGENERATING INTERVERTEBRAL DISK

The symptoms under this caption are strikingly consistent. The significant ones are as follows:

1. Chronic pain low in the back has usually existed for years. The patient consistently locates this pain in the lumbosacral region or the upper aspect of the sacrum. Often the maximal pain will be in the region of the sacroiliac joint<sup>9</sup> or located at a point about midway between the

7. Jung, A., and Brunschwig, A.: Recherches histologiques sur l'innervation des articulations des corps vertébraux, Presse méd. 40:316-317 (Feb. 27) 1932.

8. Keyes, D. C., and Compere, E. L.: The Normal and Pathological Physiology of the Nucleus Pulposus of the Intervertebral Disc: An Anatomical, Clinical and Experimental Study, J. Bone & Joint Surg. 14:897-938 (Oct.) 1932. (Note—These authors give an excellent bibliography.)

9. This common location of the pain makes it understandable that for so long the syndrome under discussion was thought to be due to a "sacroiliac strain," in spite of the totally normal roentgenologic findings and even absent ankle reflex (in cases of herniating disk). Strain of the sacroiliac joint as a diagnostic entity *sui generis* must, for the most part, be a mistaken entity and the diagnosis without foundation. Although the diagnosis is still commonly made, it must surely in time become obsolete.

sacroiliac joint and the greater trochanter of the femur. The significant fact is that the pain is not referred higher.<sup>10</sup>

2. This chronic pain low in the back may be associated with reflex pain down the posterior aspect of the thigh. Such reflex pain does not commonly extend below the knee and ordinarily is not so specifically localized to the sciatic nerve as is that which is due to compression of the nerve root. It is not uncommon for the reflex pain to be bilateral or to shift from one thigh to the other or even at times to be referred to the lateral or the anterior aspect of the thigh.

3. The episodes of pain are periodic and usually become maximal the day following some work such as shoveling snow or working in a garden. The following morning the patient complains of unusual stiffness and pain low in the back and finds it difficult to get out of bed. A common statement is that he has to crawl slowly out of bed.

Soft mattresses, which cause the patient to maintain a somewhat flexed posture in bed, are especially provocative of pain low in the back for these patients. The spinal axis at the lumbar or the lumbosacral joint is weak, and the flexed posture maintains a perpetual strain on the perispinal ligaments and erector spinae muscles, which results in pain and stiffness low in the back. Many of the patients have discovered this for themselves and have found that they fare much better by sleeping on the floor. This is understandable when one realizes that the type of backache under consideration is due to strain on the ligaments and muscles and is comparable to the pain of a stiff arthritic knee. After the patient maintains a fixed posture for a time, such as lying in bed or sitting in a chair or sitting in a theater, he experiences stiffness and pain low in the back when he attempts to straighten up. These patients find it more difficult to stay in one position than to shift or to keep moving. They are particularly "poor sitters."

4. Exaggeration of the pain on coughing or sneezing is denied or is minimal because of the absence of compression of a nerve root and the attending inflammation of the root that is associated with herniating disk. The patient does not experience various forms of paresthesia of a leg or foot for the same reason—absence of compression of a root.

On examination of the patient the various signs that one tests for in respect to herniating disk are not outstanding. Bending of the back is limited and causes pain referred to the lumbosacral joint. Spasm of the erector spinae muscles, painful straight leg raising and tenderness to hard

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10. Strictly postural backache (in otherwise normal backs) is referred to the upper part of the lumbar region, the loins and the lower ribs. It can be no better depicted than in the well known advertisements for medicines for renal disease. Such pain seldom has any relation to the kidneys but is a postural backache and is commonly induced by the half reclining posture on modern davenports and soft mattresses.

pressure on the fourth and fifth lumbar spines may be present but are not nearly so outstanding as in the case of herniating disk. One does not find hypalgesias in the distribution of the fifth lumbar and first sacral roots, and there is no absence or diminution of the achilles tendon reflexes.

Before the diagnostic features of degenerating intervertebral disk and herniating intervertebral disk are contrasted and compared, it is well to review the symptoms and signs of the latter as they are known to be at the present time.

#### IV. SYNDROME OF HERNIATING, OR RUPTURED, INTERVERTEBRAL DISK

Since the causal factor of recurring or persistent sciatic pain was pointed out in 1934<sup>11</sup> as a common entity, a great deal of study has been devoted to the syndrome of herniating intervertebral disk. The discovery of this syndrome is one of the important advances of the century and provides a solution to a serious problem of relatively high incidence. Thousands of patients have been operated on, and many reports have been made. In the earlier days, caution led to the visualization of the herniating disk by myelography with iodized poppyseed oil and air and to prolonged conservative treatment before operation was resorted to. Time and experience have led to the conclusion that chronicity, unilaterality and typical radiation of sciatic pain to a leg or ankle means herniating intervertebral disk until otherwise proved. The diagnosis has proved to be accurate in 90 to 95 per cent of cases—as high an accuracy as in the diagnosis of any nonvisualized pathologic entity. The syndrome of herniating intervertebral disk is predominantly that of pain in a nerve root because the protruding portion of the disk compresses a nerve root against the ligamentum flavum adjacent to it (see figure 1). Because 90 to 98 per cent of the pathologic disks are below the fourth or fifth lumbar vertebra, the important and usual features in the history are as follows.

Chronic pain low in the back is referred to the level of the sacrum or lumbosacral joint and is associated with pain in the region of the sciatic notch, radiating down the posterior aspect of the thigh and to the calf or lateral aspect of the leg and often to the ankle, heel, entire foot or either side of the foot. About 25 per cent of the patients deny the presence of pain low in the back and describe only sciatic pain. A small percentage of patients experience sciatic pain on both sides, and in these patients the pain is usually unilateral for some time before becoming bilateral. This is an indication that the herniation has become extensive enough to compress the corresponding roots on each side of the spinal

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11. Mixter, W. J., and Barr, J. S.: Rupture of the Intervertebral Disk with Involvement of Spinal Canal, *New England J. Med.* **211**:210-215 (Aug. 2) 1934.

canal. One of the notable features, however, concerning herniating disks is that the herniation and hence the sciatic pain are so commonly unilateral and associated with no pain whatever or at any time in the opposite extremity.

Remissions of pain are characteristic. The interval between attacks as well as the duration of the attack varies greatly. As time goes on, the attacks become more frequent and the patient comes to fear the next inevitable attack, which may be precipitated by a trivial strain or come about spontaneously. Probably one of the reasons the patient recovers from an attack is that everything is done to place the lesion at rest. Spasm of the erector spinae muscles and curvature of the spine, with tilting of the pelvis, develop to splint the spine and favor the lesion.

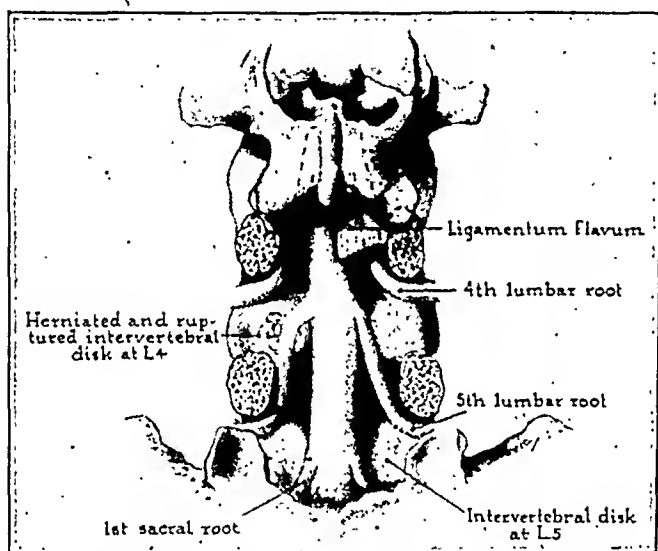


Fig. 1.—Drawing which illustrates the usual type and location of herniating intervertebral disk. The herniation of a mass of extruded nucleus compresses the overlying nerve root against the closely investing and unyielding ligamentum flavum. The ruptured herniation and extruded nuclear material shown here are of the fourth lumbar disk. Those occurring at the fourth and fifth disks are of about equal incidence.

The patient makes as few unfavorable movements as possible and may even take to bed for a few days and thus put the lesion at rest. Between recurrences of acute pain the patient may feel well or may be conscious of a residual pain of varying degree in the hip or back of the leg.

There is one occasion on which the patient takes to bed and ordinarily remains bedridden until relieved by operation. This occurs when the sequestered nucleus pulposus is suddenly extruded into the spinal canal. At operation the surgeon finds the nucleus in the canal, severely displacing the adjacent nerve root, and the nucleus often can be pulled away in one piece.

Coughing and sneezing almost invariably aggravate the pain of herniating disk. Patients often state that they have to grab hold of something when they sneeze, because pain is so terrific. This is undoubtedly due to the effect or impingement of the spinal fluid "pressure wave" on the hypersensitive, inflamed nerve root.

Paresthesia in some form is almost invariably experienced by persons with herniating disks. It is significant evidence of involvement (in this case, compression) of the sensory component of a nerve root. The patient most commonly describes or recognizes the paresthesia as a "sleepy" feeling in the leg or foot. Other interpretations are "numbness," "pins and needles feeling" and sensation of "coldness."

Patients with degenerating disks which have not herniated and those with herniating disks often have difficulty in resting at night, because of discomfort. Both classes of patients also often complain of stiff and painful backs when getting out of bed in the morning. However, it is worth repeating that there is a consistent difference in the two classes in respect to moderate activity as the day is begun. Those without herniation of the disk appreciate some relief from the pain low in the back as they "limber up," while those with herniating disks and their resulting pain from compression of the roots experience exaggeration of pain with activity.

In taking the history one should always inquire about control of the bowels and bladder in order that conditions other than herniating disk might not be overlooked, such as tumor of the cauda equina. Simple herniating disk does not affect bowel and bladder control (see section on rare and unusual cases).

*The Examination.*—The patient should unquestionably be subjected to a general examination before being operated on for herniating disk. However, he is often referred to a neurologist or neurologic surgeon for the express purpose of determining whether the diagnosis is herniating disk or not. In this respect I have found ten features concerning the examination that I feel are significant.

#### Tests Made with Patients Standing:

1. The lordotic curvature of the lumbar portion of the spine. The lordotic curvature of the lumbar portion of the spine is usually flattened. This can be determined by inspection and by a lateral roentgenogram of the lumbar portion of the spine. The patient should be stripped except possibly for a loincloth and asked to stand in his natural posture, with heels together. It is striking how commonly persons with herniating disks have flat backs and how uncommonly they present pronounced lordosis of the lumbar part of the spine. How much of this flattening is due to muscle spasm and how much is natural for the patient is difficult to say. However, one should be wary of patients with pronounced lordosis. I have operated on 3 patients (all women) who presented pronounced



lordosis. There was sufficient evidence on which to base a suspicion of herniating disk, but all 3 patients proved not to have such at operation. The causal factor for the pain in these patients is not yet clear, but it is interesting that extensive decompression of the fifth lumbar and first sacral roots on both sides was rewarded by considerable relief from symptoms. By decompression is meant extensive removal of the ligamenta flava, especially that which invests the lateral walls of the spinal canal and the proximal aspect of the intervertebral canals. This is combined with partial unroofing and widening of the intervertebral canals.

2. Physiologic scoliosis. The lumbar portion of the spine is often curved in a lateral direction to some extent. The curvature can be discerned by inspection of the patient's back as he stands. It is also evident in the anteroposterior roentgenogram of the lumbosacral portion of the spine. The curvature is a result of muscle spasm and may be either toward or, more often, away from the side of the sciatic pain. Tilting of the pelvis may develop concomitant with the scoliosis and become so prominent that one lower extremity will appear shorter than the other when the patient lies flat on his back. Such a scoliosis can be made more obvious by having the patient bend forward. He will deviate toward the concave side.

3. Spasm of the erector spinae muscles. The patient is requested to stand in his normal posture, with heels together. The examiner palpates the erector spinae muscles on either side of the lumbar portion of the spine. One can soon learn to differentiate a normal from a spastic muscle. A normal muscle can be easily indented with the tips of the fingers and has the same consistency on both sides. These muscles may become so spastic as to feel boardlike and may stand out like whipcords to inspection. There is often an unequal spasticity on the two sides. If one has the patient extend his back a little the spasticity will not be entirely relieved.

4. Bending of the back is limited and painful. The patient is asked to bend forward, backward and to each side as far as he can or until he experiences pain. Forward bending is more consistently painful, the pain being referred to the region of the lumbosacral joint and often down some portion of the sciatic distribution.

Tests Made with Patient Lying Down:

5. Patrick's test and straight leg raising test. Patrick's test is performed by the placing of the ankle of one lower extremity on the leg of the other, just below the knee. Some pressure is then made downward on the bended knee. In the case of disease of the hip joint this maneuver is usually painful, but it is almost always painless in uncomplicated herniating intervertebral disk.

The straight leg raising test is performed by an attempt to raise the straightened lower extremity to as far as 90 degrees to the body. This

test is almost always productive of pain in the back, hip or sciatic nerve and especially in the latter on the painful side. The pain is due to stretch of a hypersensitive sciatic nerve. While the test almost always gives positive results on the side of the sciatic pain, the results are just as consistently negative on the normal side.

Kernig's test is an equivalent test and is performed by first flexing the thigh on the hip to 90 degrees and then extending the leg on the thigh.

6. Circumferential measurement of the leg at the greatest bulk of the calf muscle. Particularly in long-standing herniating disks, atrophy of 1 to 2 cm. can be demonstrated on the side of the sciatic pain. The finding is consistent enough to represent a true atrophy that results from long-standing compression of the motor component of a nerve root.

7. Demonstration of hypalgesia and diminished tickle on the sole. When one becomes experienced in performing the test for hypalgesia and diminished tickle on the sole, one can practically always demonstrate a diminished sensibility to pinprick in cases of herniating disk below the fourth or fifth lumbar vertebra. An ordinary straight pin is probably the best instrument. A needle is too sharp. The skin should be pricked just hard enough so that in normal zones the element of pain is minimal. The examiner should explain to the patient that he intends to prick the skin lightly on corresponding places on the lower extremities; that he will stick just as hard on one side as on the other and that the patient is to note whether the prick is more lively on one side or whether there is no difference. It is well to start high on the thighs to accustom the patient to the object of the test. Usually his response is that there is no difference on the thighs. Then the common sites of hypalgesia are tested. The zone where hypalgesia is most consistent is the lateral aspect of the leg, about midway between the knee and ankle. The spot that best represents the distribution of the fifth lumbar root (in the case of herniated disk below the fourth lumbar vertebra; the disk at the fourth lumbar space) is the medial aspect of the base of the large toe. At times it seems to be represented at the center of the ball of the foot and that region on the dorsum at the base of the second and third toes. Sometimes this central region of the foot appears to be more hypalgesic than the mesial aspect of the base of the large toe when the fifth lumbar root is involved. At other times, the reverse is true.

The locus that best represents the distribution of the first sacral root (in cases of herniating disk below the fifth lumbar vertebra, the disk at the fifth lumbar space) is the lateral aspect of the foot at the base of the small toe.

I feel that the important issue consists in clearly establishing hypalgesia in one or more of these significant loci on the foot and thus confirming the possibility of herniation at the fourth or fifth lumbar disks or both.

I have not yet convinced myself that one can differentiate between the fourth and fifth lumbar disks by the sensory test or by the status of the ankle jerk sufficiently to guide the surgeon in his exploration of one to the exclusion of the other.

I have observed that the sensation of tickle when the sole is lightly stroked is about as consistently diminished as sensibility to pinprick on the side of the pathologic changes.

8. Tenderness of the spine and loins. The patient is asked to turn on his side. Firm pressure on the fourth or fifth lumbar spines is often painful. Just as often, pressure in the loin lateral to the lumbar portion of the spine is painful on the side of the sciatic radiation and is not painful on the normal side.

9. Tenderness of the sciatic nerve and calf muscle. The patient is asked to lie on his stomach. With pressure along the course of the sciatic nerve with the finger tips, tenderness or soreness of the nerve on the painful side will be noted by the patient. Likewise, the calf muscle will be tender on squeezing on the painful side when compared with that on the normal side.

10. Patellar and achilles reflexes, or knee and ankle jerks: While the patient is lying on his stomach, he should adjust himself so that his feet extend beyond the end of the examining table. It is well to put slight pressure on the ball of the foot while the achilles tendon is briskly tapped. If there is any doubt about the equality of the reflexes on the two sides or if they are both absent, the patient should be placed in the optimum position for testing the ankle jerk. He should kneel in a chair and face the back of the chair. The ankles only should clear the chair and should be relaxed. If both ankle jerks are absent, reenforcement should be tried by the patient's clasping his hands and pulling while the test is being made. Sometimes one can bring out a diminished ankle jerk on one side by repeatedly tapping the tendon in moderately quick succession. On the side of the pathologic changes the reflex will "wear out" after three or four taps, while it persists indefinitely on the normal side. It is also helpful to try the minimal force of the reflex hammer that will cause a reflex response. Small differences in the response on the two sides can be effectively demonstrated in this way. That is, the minimal tap which causes a response on the normal side may fail to evoke a response on the affected side. Tendon reflexes are so consistently equal on the two sides in a normal subject that any definitely proved diminution on one side, however small, is significant.

I have only rarely encountered a patient who presented a diminished knee jerk that was due to chronic intraspinal herniation at the fourth or fifth lumbar disks. Such a finding should certainly cause one to consider the possibility of a caudal tumor, a herniating disk at a higher lumbar seg-

ment or some other lesion. However, I have operated on 2 patients who presented definitely diminished knee jerks and absence of ankle jerks on the painful side. The sciatic pain in both patients was severe, of sudden onset, unrelenting and of only two to three months' duration to the time of operation. Both patients also complained of numbness and hypalgesia to pinprick as high as the second lumbar distribution on the painful side. Both presented extrusion of sequestered nuclear material through erosions in the annulus at the fifth lumbar disk, and there was no herniation or other lesion at a higher level. The knee jerks became equal some weeks following operation. This teaches only that an acute severe compression of a nerve root may cause a depression of the deep reflex at a higher level as well as hypalgesia at a higher level.

I have encountered 2 patients who presented diminished knee jerks due to herniation of the fourth lumbar disk into an intervertebral canal, with consequent compression of the fourth lumbar root (see extended exploration for herniation in an intervertebral canal).

About 50 per cent of the patients with herniating disks at the fourth or fifth lumbar vertebrae will present diminished or absence of ankle jerks on one side. I have encountered a few patients who presented an absence of ankle jerk on the side opposite to the sciatic pain. I have recently operated on a patient whose ankle jerks were equal a few days before operation. At the first examination, five months before, when sciatic pain had first appeared and was severe, the right ankle jerk could not be elicited. There was a pronounced herniation at the fifth lumbar disk on the right. Hence, if an ankle jerk is not diminished at the time the patient is examined, it does not necessarily follow that this was so at the time when sciatic pain was acute.

These detailed remarks concerning the ankle jerks have been made purposely because an ankle jerk is an important sign. Misinterpretation can easily be made by persons who have not particularly trained themselves in the obtaining of reflexes. In cases of unilateral, chronic or recurring pain in the sciatic distribution and in patients who present some of the symptoms and signs as described, a diminished ankle jerk makes the diagnosis of herniating disk mandatory until otherwise proved. The finding is, of course, not necessary for the diagnosis.

One should always include in the examination at least the tests for the abdominal, cremasteric and plantar reflexes and for genital and perianal sensibility. Abnormal responses may give a clue to other and rarer types of pathologic changes.

#### V. RARER SYMPTOMS AND RARER CASES OF HERNIATING INTERVERTEBRAL DISK

1. *Pain in the Back of the Neck Due to Herniating Lumbar Disk.*—I have seen 6 patients who complained of pain in the back of the neck, in

addition to other symptoms. This caused some confusion at first, but the symptom disappeared with the others after operation. It is undoubtedly due to spastic erector spinae muscles, the effect of the spasticity reaching as high as the back of the neck. Some of these patients complained of headache, which disappeared along with the other symptoms after operation. Stiffness and pain in the muscles of the back of the neck could logically have provoked a generalized headache.

2. *Acute Rupture of a Part of the Nucleus Pulposus Without Antecedent Pain Low in the Back or Other Symptoms.*—There have been 8 cases of rupture of part of the nucleus pulposus without antecedent symptoms in my practice. The duration of the symptoms has been two weeks to one year until the diagnosis was made. Either the patient was confined to bed from the sudden onset of sciatic pain, or else the latter maintained its intensity until the sequestered nucleus pulposus was removed. The pain was excruciating, and the straight leg raising test gave definitely positive results. In most of the patients the entire lower extremity seemed painful. That is, the patient did not refer the pain as strictly to the course of the distribution of the sciatic nerve as does the usual patient with herniating disk. In cases of more insidious development the sciatic pain is more delineated. Also, in acute cases, the whole lower extremity is likely to be hypalgesic. This is not out of keeping with altered sensibilities when the onset of pain is sudden and excruciating. The following are illustrative cases.

CASE 1.—H. D., a youth aged 17 years, was admitted to St. Joseph's Hospital, Denver, on June 27, 1945. He experienced sudden sciatic pain radiating to and involving the calf muscle on the left side only. The incident occurred one year before, when he lifted a heavy object and the pain persisted. He denied the presence of pain low in the back either before or after the onset of sciatic pain. There were the usual symptoms and signs of herniating disk. At operation, a pronounced herniation was disclosed on the left side of the fifth lumbar disk. It displaced the first sacral root and severely compressed it against the ligamentum flavum. When the root was dissected and reflected mesially, the disk capsule ruptured spontaneously and a sequestered portion of the nucleus extruded itself. It came from a well formed pocket, and I estimated that only about one third of the nucleus had sequestered. The rest of the disk was firm and of normal integrity. Relief was immediate and recovery uneventful.

CASE 2.—W. M., a white woman aged 24 years, was admitted to St. Joseph's Hospital on July 12, 1945. She had experienced the sudden onset of pain which radiated typically in sciatic distribution from a point midway between the lumbosacral junction and the great trochanter of the femur<sup>12</sup> down to and involving the heel and instep of the right foot. The incident occurred while she was skiing six months before. She denied pain in the left lower extremity and denied pain low in the back either before or after the onset of sciatic pain. She presented the usual symptoms and signs of herniating disk. At operation,

12. This is such a common locus for the pain of herniating disk that for the sake of brevity I have designated it as "point A."

a completely sequestered and pocketed rupture was disclosed on the right side of the fifth lumbar disk. I estimated that one third to one half of the nucleus had sequestered and that the rest of the disk was of normal integrity. Only the fifth lumbar disk was explored.<sup>13</sup> Recovery was uneventful, and she was discharged, completely free of pain.

CASE 3.—V. G., a white woman aged 33 years, was admitted to St. Joseph's Hospital on June 26, 1944. While moving a rock about three months before, she "wrenched" her back. She denied pain low in the back previous to this incident. The lower part of the back continued to ache, and three weeks before hospitalization she felt sudden pain, which radiated typically in sciatic distribution to and involving the right ankle. She denied pain in the left lower extremity. She presented the usual symptoms and signs of herniating disk excepting the fact that the achilles reflexes were equal. At operation, a pocketed and completely sequestered portion of the nucleus was found on the right side of the fifth lumbar disk. I estimated that about one fourth to one third of the nucleus had sequestered and the rest of the disk was of normal integrity. She made an uneventful recovery and was discharged free of pain. It is of interest that she experienced the sciatic pain while her husband was convalescing from an operation for herniating disk.

It is interesting to note that the first 2 patients were relatively young. It has been my observation that in the more youthful patients the complaint of pain low in the back, if any, accompanying sciatica is less prominent than that in older patients. This raises the conjecture that partial sequestrations may tend to progress to completion more rapidly than complete degeneration of the entire disk.

The nature of the pathologic change and its development, especially in such young patients, when contemplated in all its aspects, favors the contention that the disintegration and sequestrations are on a developmental basis. It is true that these patients dated the acute onset of sciatica to a strain of the back, but a study of the pathologic changes makes it obvious, I feel, that the strain was only an incidental and a precipitating factor; that is, the strain was associated with sufficient stress to disrupt a pre-existing weak and degenerating disk.

I have recently examined a boy 9 years of age who experienced the sudden onset of typical sciatic pain on one side, which confined him to bed, and who presented all the symptoms and signs of herniating disk. He denied pain low in the back and could not recall ever having sprained his back. He has not yet come to operation.

3. *Absence of Achilles Reflex on the Side Opposite That of Sciatic Pain.*—The combination of the absence of the Achilles reflex on the side opposite that of the sciatic pain has already been mentioned. There have been 4 cases in my experience, and, as might be suspected, the disk was herniated clear across the spinal canal, so that the nerve roots on each

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13. In a case of this kind, in which there is sudden onset of sciatic pain uncomplicated by long-standing pain low in the back and sufficient pathologic change found to explain the syndrome, I feel that one can reasonably forego exploration of the fourth lumbar disk.

side were compressed. Though the phenomenon seems strange, the only explanation is that the sensory component of the nerve root on one side bore the brunt of compression while the motor component sustained it on the other side.

4. *Large Ruptured Disk with Complete Caudal Lesion.*—There have been only 3 cases in my experience. The findings were those typical of complete caudal lesion at the fifth lumbar disk, anesthesia in the distribution of the first sacral roots down, absence of achilles reflexes and paralysis of the rectal and vesical sphincters. All patients made slow recoveries after operation.

5. *Symptoms of Herniating Disk Referred to Phantom Extremity.*—A man of 60 had an amputation high in a thigh thirty years ago because of a crushing injury to the leg. The stump was good, and though he sensed the presence of the phantom leg he never experienced pain. Six months ago pain low in the back and typical sciatic radiation to the phantom foot began to develop. The stump was not locally tender, but flexion on the hip aggravated the sciatic radiation. Though the patient has not yet come to operation, I am convinced that he has a herniating disk on the side of the amputation.

6. *Pain in Only the Foot and Leg.*—There have been 2 patients who complained of pain only in the ball and instep of the foot and pain in the lateral aspect of the leg on one side. They described the pain as beginning in the foot and going up the leg. The foot was tender and sensitive, so that stepping on it or putting it into a shoe was painful. They had been from place to place, acquiring different types of shoes and getting repeated roentgenograms of the foot, the latter being always normal. The fact that they never complained of pain low in the back or pain above the knee made the correct diagnosis obscure and unsuspected. When they described, located and traced the course of the pain, however, the distribution of the single root was betrayed. This together with paresthesia, hypalgesia in root distribution and diminished ankle jerk established a diagnosis. Persistent pain in a foot and perhaps leg, especially when unilateral and when no other cause can be found, should arouse the suspicion of a herniating disk.

7. *Pain in the Rectum.*—I have seen a few patients who complained of pain in the rectum and pain on defecation at times. No local cause for the pain could be found. The complaint was in addition to those related to a herniating disk, and it disappeared after operation. I have suspected that it might be due to spasm of the levator ani muscles and other muscles of the pelvic floor, being on the same pathophysiologic basis as spasm of the muscles about the lumbosacral and sacropelvic regions.

8. *Signs Contaminated by Lesions of the Upper Motor Neuron.*—There have been 2 cases with lesions of the upper motor neuron in my

practice. In 1 there was a Babinski sign on the side of the herniation of the disk due to an old injury of the spinal cord. The herniating disk was at the fourth lumbar space. In the other case there was a Babinski sign and a hyperactive knee jerk and ankle jerk on the side of the sciatic pain. The hyperreflexia was due to an old injury to the brain. In such cases the diagnosis of herniating disk at the fourth or fifth lumbar space is more difficult. However, the description of typical sciatic pain and the demonstration of hypalgesia in the fifth lumbar or first sacral distribution is strong evidence for herniating disk. One should not let the disturbing signs of the upper motor neuron eliminate the diagnosis, providing there is clear evidence for the existence and cause of the independent lesion. The cause of the signs of the upper motor neuron must, of course, be established also. In the 2 cases in my experience they were due to old injuries.

#### VI. THE ROENTGENOGRAM

Unfortunately, there is little in the ordinary roentgenogram of the lumbosacral portion of the spine that would substantially warrant the diagnosis of herniating disk. Narrowing or collapse of a disk arouses interest. I am not yet convinced concerning its reliability as a pathognomonic sign. I have operated on several patients who presented complete collapse of disks in the roentgenograms. One was in the cervical region, between the sixth and seventh cervical disks, and no herniating disk was found. In 1 case, that of a woman (O. H.) 48 years of age, the patient complained of pain low in the back which had been a severe handicap to her for twenty-eight years. She had experienced radiating pain to the calf muscles on both sides and sensations of numbness in both legs. The roentgenogram showed an almost complete absence of the intervertebral disk at the fourth lumbar space (see figure 2). At exploration, no rupture of the disk was found. A bulging annulus was present, which narrowed the spinal canal. When the annulus was incised no nucleus pulposus could be found. The vertebrae were closely opposed but not fused. Compression of the roots could be attributed to the bulging annulus and to the narrowing of the intervertebral canals. In such cases, the nerve roots might properly be widely decompressed and the bulging annulus excised, as was done in this patient. The result was good, with pronounced alleviation of the long-standing symptoms. I cannot explain the loss of disk substance, but it was not herniated into the spinal canal.<sup>14</sup> I feel that this represents a congenital anomaly and that the nucleus failed to develop embryologically. It is hardly conceivable that the nucleus could have been "absorbed." If this were possible, then more such exam-

14. See discussion on "extended exploration for herniation in an intervertebral canal" under section on "operation." Information concerning herniation and rupture of the intervertebral disk anteriorly is as yet meager.



ples should certainly have been encountered among the large number of degenerating and herniating disks that have been explored.

There has been only one exception to the rule of normal roentgenograms. In herniations that have been present for many years a posterior lipping of the vertebrae may occur, that is, a sizable cone of bone develops around the base of the protruding disk. This was demonstrated in the roentgenogram in 2 patients, 1 of whom had symptoms for twenty years. After examining many roentgenograms, I have been unable to find any other incontrovertible clue to the diagnosis. Physiologic scoliosis and

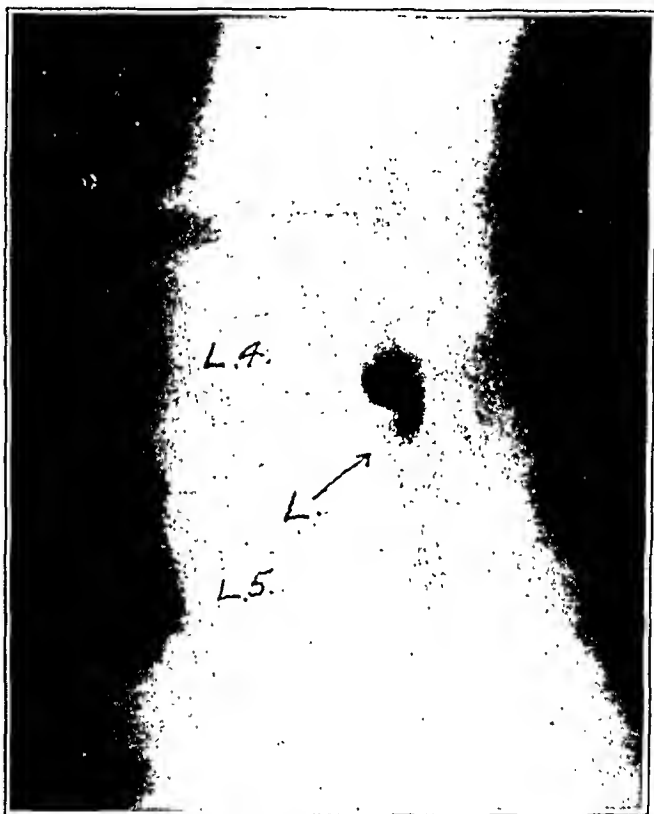


Fig. 2.—Roentgenogram of the lumbar portion of the spine in the case of O. H. Note the close approximation of the fourth and fifth lumbar vertebrae. The bony lipping at *L* together with a bulging annulus narrowed the spinal canal and crowded the fifth lumbar roots. The vertebrae were not fused, but tissue resembling nucleus pulposus could not be found. This is probably a developmental anomaly and not due to absorption of a nucleus pulposus.

diminished or absence of lordosis are commonly associated with herniating disks but are only contributory in value.

However, the anteroposterior and lateral views of the lumbosacral portion of the spine should always be taken before operation is resorted to, if only to rule out skeletal pathologic changes. This precaution has saved me the embarrassment of exploring several metastatic neoplasms.

Spondylolisthesis may be responsible for a syndrome that simulates herniating disk, but the surgical indications are different from those related to herniating disk.

In 1941 I attempted to find some roentgenologic means whereby one might establish the presence of a soft, degenerating disk. With the idea that an abnormally soft disk might be more compressible than the normal, controlled roentgenologic studies were made as follows: Lateral exposures of the lumbosacral portion of the spine were taken, the exposure being centered through the fifth lumbar disk. Exposures were made with the patient in the erect posture and when hyperextended and when hyperflexed. Normal subjects and patients with disks which were later proved to be degenerating and herniating were studied. Careful measurements of the changes in the width of the disks with the extremes of posture were made. The most pronounced change in the shape of the intervertebral disks was associated with the flexed posture. When the patients changed from erect posture to extreme flexion, the distances between the anterior lips and the posterior lips of adjacent vertebrae changed sufficiently to provide substantial measurable differences. However, I was unable to establish an index of change that had sufficient value in differentiating the normal from the abnormal. The normal findings in no way discredit the concept of the soft disk and the unstable joint. The joint may be considerably weakened without providing gross dependable changes in measurements of disks in this experiment.

In earlier days, when an understanding of the syndrome of herniating disk was in a nebulous state, congenital malformations of the lumbosacral part of the skeleton gave much concern. Such were sacralization of the fifth lumbar vertebra, elongation of the transverse process of the fifth lumbar vertebra, variation of the articular facets and defects of the neural arches. Experience has led to the conclusion that given a syndrome of herniating disk these skeletal malformations may ordinarily be disregarded. Furthermore, the incidence of such malformations in painless backs is high.

A patient with a syndrome of degenerating or herniating disks may reveal a mild or moderate degree of lipping, especially of the lumbar vertebrae. One should not be too hasty in attributing the symptom complex to arthritis and in relegating the patient to the limbo of the lost. Arthritis has tended to become a diagnostic panacea when other causal factors for symptoms are not understood. The "x-ray arthritis" is likely to be only incidental, especially when a patient has no pain or symptoms above the lower part of the back. In any case, a patient deserves thorough investigation before being labeled "arthritic."

In follow-up roentgenograms about three to four months after thorough curettement of a disk, I have found that the disk space will commonly but not always become narrower by about one third of the

space shown preoperatively. In 1 patient it decreased by one half. I have not found one to collapse completely. Up to one year after operation I have yet seen no evidence of ossification of the disk. Keyes and Compere<sup>8</sup> reported a case of ossification of the nucleus pulposus, but it must be rare. They pointed out that only the epiphysial ring (the rim around the vertebral body that is adjacent to a disk) has bone-forming properties. This may explain the uncommon ossification of the disk and the relatively common lipping or spur formation. Indeed, the new bone may be a traction spur, which indicates an excessive strain at the junction of the vertebral rim and the annulus. This may possibly indicate a weakness and an inefficiency of the intervertebral disk (see case of A. H., under extended exploration for herniation in an intervertebral canal in the section on operation).

*Recapitulation.*—The thesis presented in this paper involves only going back a step and recognizing that the intervertebral disk must undergo degeneration before it herniates and ruptures. When it is undergoing the process of degeneration, it serves as an inadequate and inefficient joint. As a result of this, undue stresses and strains are placed on the perispinal and lumbosacral ligaments and muscles. This, in turn, is the cause of pain low in the back. It is more likely that strain of the short ligaments is the cause of the acute pain, while muscle spasm is secondary. The mechanism of the acute pain or "catch," which is so commonly parasacral, is not unlike that of a sprained ankle. In time, the annulus fibrosus, or the tough capsule which encases the nucleus pulposus, becomes so thin and inadequate that it can no longer retain the nucleus pulposus under strain and consequently herniates and finally ruptures, extruding the sequestered nucleus into the spinal canal. Concomitant with this the nerve root adjacent to the disk is compressed and the symptoms and signs of compression of the nerve root supervene—to wit, radiating pain in the sciatic distribution, pain on coughing and sneezing and paresthesias.

The statement that "in time the annulus gives way to herniation" may be modified in the light of this observation: The incidence of the "weak lower part of the back" is high, and the severity of pathologic changes and symptoms varies considerably from a mild degree to one which is a serious handicap, because of both chronic pain and a physical incapacity for labor and for making a livelihood. However, many of the afflicted persons never progress to the stage of severity that would reasonably demand operation. The process of degeneration may be slow or may possibly even become quiescent. The nature of the patient's activity may be such that he makes no great demands on his back and he adjusts his life and activity so that in spite of the defect he can live his normal life in relative comfort. In some instances the degeneration progresses to complete dissolution of the disk, and this may obtain

spontaneously without postulation of the factor of trauma or strain. But, obviously, many patients never progress to this stage and never require surgical intervention. In cases of moderate severity, the patient may be relieved temporarily or permanently by the aid of some partially stabilizing appliance such as a suitable corset or brace. In any case, I feel that this chronic deficiency low in the back is in the majority of cases due to pathologic changes in the intervertebral disks, which are probably of a developmental origin. Given such a defect, they may or may not progress to a stage of severity that warrants surgical intervention. This is determined by symptoms and by the attitude and election of the patient. When one is formulating the diagnosis, prognosis and advice to the individual patient, I think that it is helpful to have this concept in mind.

To summarize, the distinction must be made between a degenerating disk and a herniating disk. The symptoms and signs of the former are those related to an inadequate syndesmotic joint, which renders an instability of the lumbosacral portion of the spine. Strain on the periarticular structures is the cause of the symptoms. When the nucleus pulposus herniates, the symptoms and signs of compression of the nerve root are superimposed.

#### VII. PATHOLOGY

In order to understand and recognize the characteristics of the degenerating or pathologic intervertebral disks, one should be well acquainted with normal disks. Studies of normal and pathologic disks are being made in collaboration with Dr. Charles B. Kingry, acting pathologist for St. Joseph's Hospital. The objectives are, first, to study the gross and microscopic characteristics of normal intervertebral disks in each decade of life and, second, to attempt to establish some criteria by which the degenerating disks can be not only differentiated microscopically from normal disks at any given decade but graded in respect to early, moderate and advanced degeneration. We feel that it is more appropriate to report the results of these studies in a separate communication. However, for the purpose of this report a brief discussion of the essentials is as follows: The normal intervertebral disk is white. It is classed as a symphysis type of amphiarthrotic joint. It is composed of three essential elements: (1) the nucleus pulposus, (2) the annulus fibrosus and (3) an upper and lower hyaline cartilage plate.

The nucleus pulposus is a centrally placed amorphous mass of tissue which has a pearly translucency (see figure 3). In the fresh state it appears wet and jelly-like, and yet one is surprised to find its degree of toughness if an attempt is made to cut or curet it away. Fluid does not seep from the cut surface. It appears to be lobulated, so that it reminds one of boiled tapioca. It is easily compressible, like fine-meshed sponge rubber, and is resilient, so that it resumes its former shape. It

is difficult to compare it with any other known structure; the nearest comparison I can make is to partially hydrated gelatin. The nucleus pulposus is evidently under great tension in youth and middle age. Figure 3 is a photograph of one half of a section of spine cut through the sagittal plane. When the specimen was cut, the nucleus bulged about  $\frac{1}{4}$  inch (0.6 cm.) from the cut surface in each half. It is this resilient fluid structure that makes possible the mobility of the spine and provides the cushioning effect necessary to the lengthening and shortening of the spine. In a newborn infant the nucleus is soft and mushy and well delimited from the annulus fibrosus and does not appear to be under great tension. In old age it loses its compressibility and resiliency and becomes less differentiated from the annulus. In youth and middle age it appears as that shown in figure 3. It is important

#### EXPLANATION OF FIGURES 3, 6 AND 7

Fig. 3.—Photograph of vertebral column cut through the midsagittal plane, showing the third, fourth and fifth lumbar and first sacral vertebrae with intervertebral disks. The specimen was taken at autopsy from a man 35 years of age, who died of peritonitis. There was no history of pain low in the back, and the spine is considered to be normal. The specimen was photographed in the fresh state.

*L. 4* indicates the fourth lumbar vertebra; *A. L. L.*, the anterior longitudinal ligament (firmly attached to disk and vertebra); *A. F.*, the annulus fibrosus; *N. P.*, the nucleus pulposus; *C. P.*, the cartilage plate, and *P. L. L.*, the posterior longitudinal ligament (attached to the disk but unattached to vertebral body; it adds relatively little strength to the annulus fibrosus).

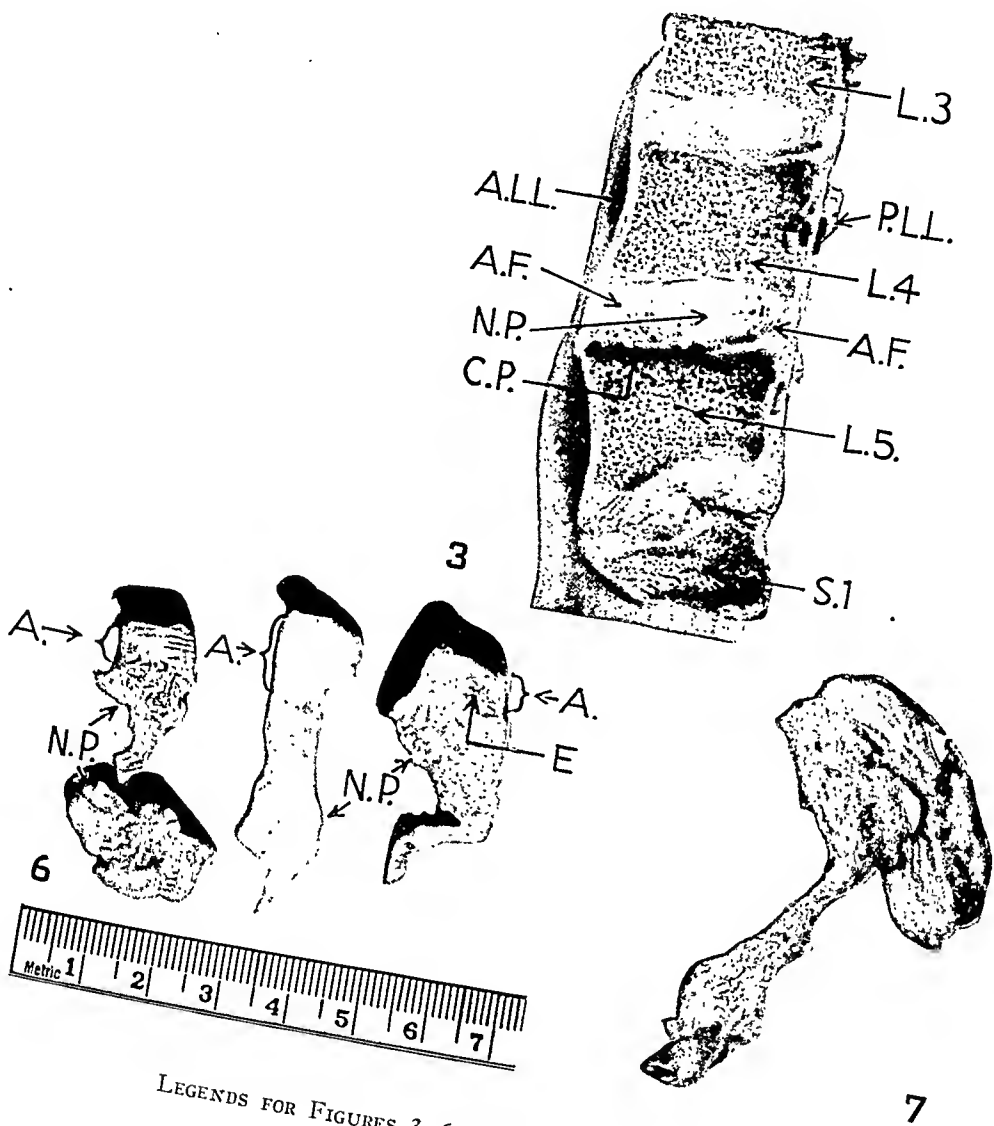
Note the bilobed character of the nucleus pulposus between *L. 5* and *S. 1*—a developmental defect.

Fig. 6.—Photographs of specimens from intervertebral disks (photographed in the fresh state). The specimens were cut from the disks posteriorly with a sharp-pointed blade. The central specimen is from a normal disk (taken from the fourth lumbar disk in the specimen shown in figure 3) Note the normal thickness and laminated structure of the annulus (*A.*) and the translucent homogeneous character of the nucleus pulposus (*N. P.*).

The two end specimens were taken from a white woman 28 years of age. She complained of severe chronic pain low in the back without sciatic radiation. Both the fourth and the fifth lumbar disks were degenerating, and after thorough curettement a good result was obtained. The specimen on the left was taken from the fourth lumbar and the one on the right from the fifth lumbar disks. Note the beefy red color of the tissue. The annulus (*A.*) has been greatly thinned and has lost its laminated structure. Note the complete erosion at *E.* Herniation and rupture of the nucleus would undoubtedly have occurred at this locus in a relatively short time.

This is probably an example of a rapid degenerative process. In time this nucleus would become drier and more fibrous and would sequesterate. Not all degenerating disks are red. This appears to characterize some of the earlier and more acute degenerations.

Fig. 7.—Photograph of a block from a degenerating disk at the fourth lumbar space in a patient who complained of severe chronic pain low in the back with reflex sciatic pain. By reflection of the dura first from one side and then the other, a block of tissue was removed, which represented the entire width of the disk. The nucleus and most of the degenerating annulus were beefy red in appearance. Note the complete erosion in the central region of the annulus. The overlying annulus at this location had the thinness of tissue paper, and mild herniation had already begun.



LEGENDS FOR FIGURES 3, 6 AND 7 ON OPPOSITE PAGE.



to note that the normal nucleus in youth and middle age is not friable, mushy, fibrous or stringy and does not come away in large pieces or fragments if one attempts to pull it with a tissue forceps or hemostat.

Keyes and Compere<sup>8</sup> pointed out that until birth the notochord serves as the chief source of the nucleus, but in a 4 year old child notochord cells are difficult to find, since they have undergone mucoid degeneration. The inner aspect of the annulus fibrosus contributes the fibrous tissue found in the nucleus and enlarges it. This process of maturation, by replacement of the gelatinous mucoid material with interspersed cells of fibrocartilage from the annulus, progresses continually throughout life until the senile intervertebral disk loses its gelatinous character and resiliency.

The annulus fibrosus is a laminated structure that encases the nucleus pulposus and has almost the toughness of leather. It is thin, superior and inferior to the nucleus, for the latter is well supported by the cartilage plates and vertebral bodies at these loci. The annulus is evident anteriorly and posteriorly where a strong capsule is necessary to retain the nucleus. It is about  $\frac{1}{4}$  inch thick posteriorly and about  $\frac{3}{8}$  inch (1 cm.) thick anteriorly at the fourth and fifth lumbar segments.<sup>15</sup> The laminae of the annulus are of fibrocartilaginous structure and are so arranged that the fibers of adjacent laminae progress in opposite directions and criss-cross or interlace each other. This arrangement provides the annulus with the unique property of being bendable, so that with change in posture of the spinal column it may bulge and retract like the bellows of an accordion and yet maintain adequate toughness and strength to retain the nucleus pulposus.

*The Degenerating Disk.*—The degenerating intervertebral disk is evident to macroscopic observation. The nucleus pulposus loses its translucency and evidently most of its water content. It undergoes a process of sequestration so that ultimately it becomes completely segregated from its confining structures and can be easily lifted in toto from its bed with tissue forceps. For convenience, I have referred to this as a "ripe" disk, because of the similarity to a "ripe" cataract. In the process of sequestration the nucleus becomes fragmented and stringy, so that large pieces may be pulled away with forceps. The fragments appear dry when compared with the glistening opalescent and wet appearance of the normal nucleus (see figures 4 and 10).<sup>16</sup>

15. The annulus is thicker in front than behind in the cervical and lumbar regions, thus accounting for the lordotic curvature in these parts. It is of about equal thickness anteriorly and posteriorly in the thoracic part of the spine. The kyphotic curve of the latter is due to a difference in thickness of the vertebral bodies in the anterior-posterior direction.

16. Karl Neubeurger (University of Colorado School of Medicine) gave suggestions and aid in the preparation of the pathologic material for study.



Microscopic examination reveals that the mucoid structure of the nucleus is replaced by fibrocartilage to varying degrees. Instead of the nearly homogeneous matrix of the normal nucleus, one finds more distinct fibers. These fibers are the product of fibrocartilaginous cells and contain some collagen. They are exhibited better by the Van Giesen stain than by the usual hematoxylin-eosin stain, and I feel that the former is of greater value in studying and grading degeneration of disks. In one specimen the fibrocartilaginous tissue progressed to actual carti-

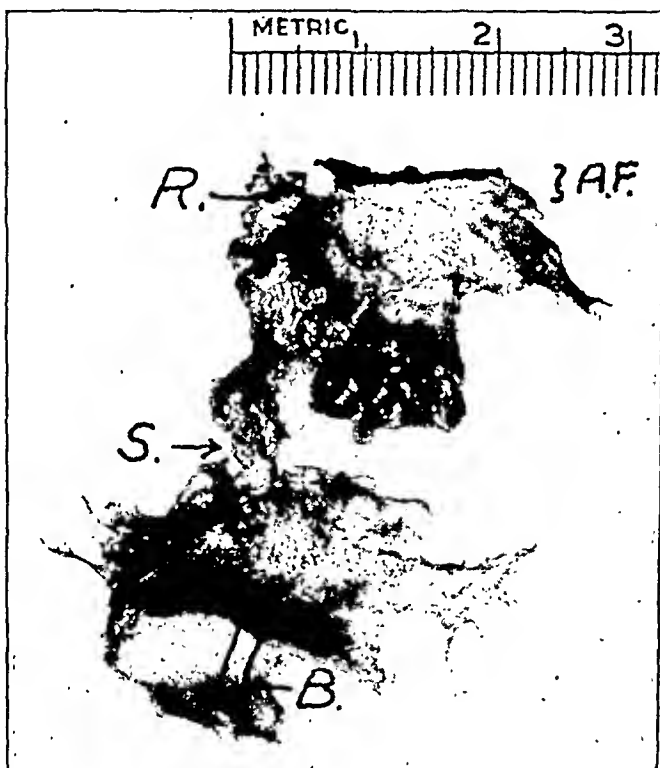


Fig. 4.—Photograph of unfixed specimen taken at operation from the fourth lumbar intervertebral disk in a man 27 years of age. The upper half of the specimen was cut "in block" from the disk and lifted out. The lower half of the specimen was a completely sequestered portion of the nucleus pulposus, attached to the upper half by only a strand of tissue (*S*). *A.F.* indicates the degenerating annulus fibrosus (the intraspinal aspect) and *R.* the rupture through the annulus where nuclear material was extruding and compressing the adjacent fifth lumbar nerve root.

Note the dry appearance of the sequestered nucleus and the frayed stringy margins. The degenerating nucleus was beefy red in color except for a few streaks of white tissue running through it. A block was taken through one of these white streaks at *B* for microscopic study. The white tissue proved to be cartilage metaplasia, while the red tissue proved to be dense fibrocartilage. A photomicrograph from this block is shown in figure 5.

laginous change in places (see figure 5). I have observed this in only one instance. I have never seen microscopic evidence of inflammation or necrosis in a degenerating disk.

The annulus also degenerates, losing its laminated appearance and structure (see figures 4, 6 and 7). It ultimately becomes so thin and inadequate that it can no longer retain the sequestering nucleus, and the latter is extruded into the spinal canal. The significant fact is that the process of degeneration involves and extends into the annulus and destroys its normal structure. Complete erosion usually occurs first in a limited and small area, and it is at this locus that herniation, rupture and extrusion of the nucleus take place (see figures 4 and 7). When dissolution of the annulus occurs, the syndesmotic joint between the

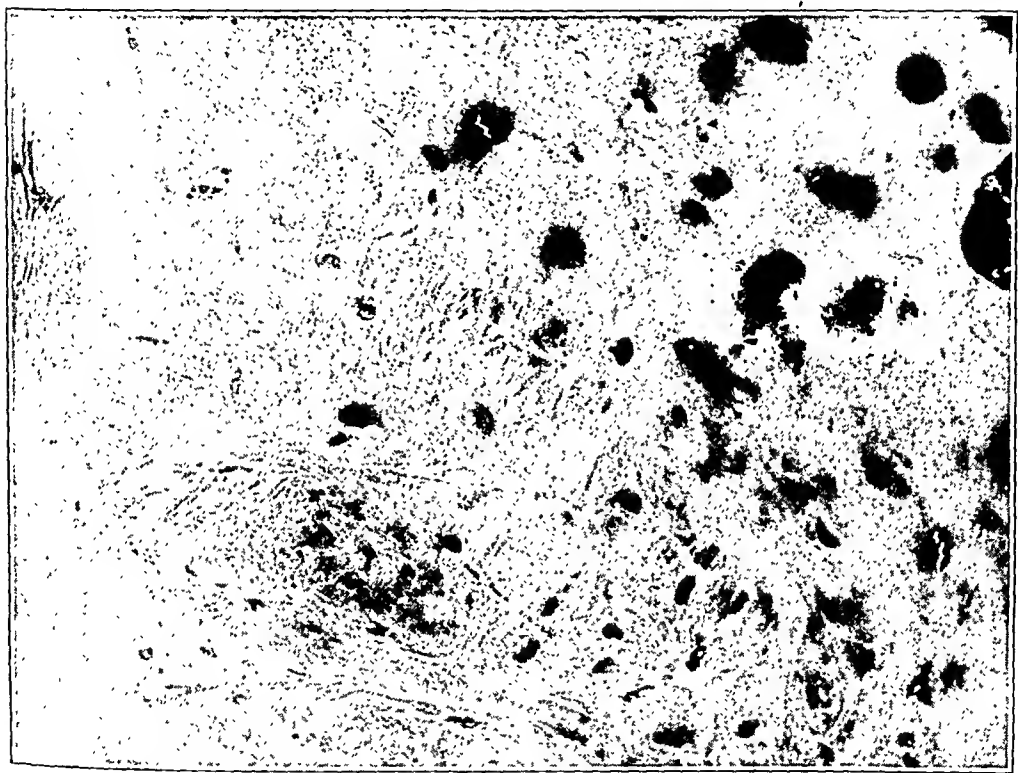


Fig. 5.—Photomicrograph of a section taken from the block (B) in figure 4. Hematoxylin-eosin stain was used. The section shows dense fibrocartilage which has undergone cartilage metaplasia on the right. This is the only instance of dense cartilage metaplasia which I have encountered in a degenerating disk.

two adjacent vertebrae is weakened and can no longer maintain the essential axial strength and stability of the spine at that joint. Other structures in and about the spine must then support its integrity with every change in posture. One might say that the fulcrum of the levering forces is proportionately transferred to the articulating joints and perispinal ligaments and remotely to the perispinal muscles. The process of degeneration is undoubtedly a slow one, measured probably in terms of years. If the annulus maintained its normal structure and the nucleus alone degenerated, I doubt that the latter could ever herniate and I doubt

that the patient would experience the symptoms of the weak lower part of the back.

It is because of these observations and because of the probability that the degenerative process may likely progress to involve the entire disk that I have felt it advisable (in most cases)<sup>17</sup> to remove as much of the nucleus as possible and to remove all the annulus posteriorly, approaching it from both sides of the spinal canal. This thorough removal of the pathologic portions of the disk prepares the way for the development of a firm fibrocartilaginous scar in the cavity that is left, thus establishing a fusion at the place where it should be made. That such a scar does develop has been proved by direct observation in the following case:

L. I., a white woman aged 29 years, was admitted to the University Hospitals, Iowa City, in January 1943. She complained of severe chronic pain low in the back, with exacerbations off and on for four years. She referred the pain to the region of the lumbosacral joint and denied sciatic radiation. Examination indicated a stiff, painful lower part of the back, with spasticity of the erector spinae muscles. The thighs were somewhat tender on squeezing, but there were no signs of compression of the nerve roots. Roentgenograms of the lumbosacral portion of the spine were normal. An impression given by the Department of Orthopedics, State University of Iowa College of Medicine, was chronic lumbosacral strain.

A laminectomy was done on Feb. 4, 1943, and the disks at both the fourth and fifth lumbar spaces were found to be degenerated. The annulus was thin and soft, and a tissue forceps could be plunged through it as easily as one can puncture a sheet of paper. There was no herniation or compression of the root by inspection. The annulus was cut away, and both disks were thoroughly curetted. The histologic examination was reported as showing degenerated and hyalinizing fibrocartilage. The patient made an uneventful recovery and in twenty-five days stated that she was free of pain. She was gratified with the result and "felt like she had been given a new back."

Three months later she returned to the hospital, complaining of the development of a relatively acute pain low in the back. She presented the symptoms and signs of what I should now recognize as being the result of a ligamentous strain, with its associated muscle spasm. Such an episode occasionally occurs even as long as two or three months after operation and is attributable to an (as yet) insufficiently stable lumbosacral portion of the spine. For this type of fibrocartilaginous fusion one should think of results in relation to the magnitude of the element of time in at least the same terms as one would for a tibial bone graft across the lumbosacral joint. This is especially true when the use of body casts is being avoided. The patient referred to here would now be treated conservatively to tide her over the acute episode. But at that time, not being informed on all the factors, I felt that it was advisable to reexplore the wound.

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17. In cases in which a small portion of the disk has undergone complete sequestration (pocketed type) and the rest of the disk appears firm and of normal integrity, one is licensed to feel that the degeneration was only partial and localized and has progressed to completion. In this instance the remaining disk is not incised.

*Reexploration.*—The soft tissue scar was tough and firm. No dead or fluid spaces had persisted. A firm and tough fibrous scar had developed across the interlaminar spaces. The dura was somewhat adherent to the overlying scar but could be separated by a blunt instrument with relative ease. The dural sheaths of the nerve roots could be reflected likewise from the disks and vertebrae with ease. The intervertebral cavities which remained after curettement three months ago were now completely filled and replaced by pearly white fibrocartilaginous scar tissue. By inspection I did not feel that the intervertebral spaces had decreased to any appreciable extent in the direction of the spinal axis. It was relatively difficult to plunge a pointed stab blade into the new disk. The one at the fifth lumbar space appeared homogenous throughout, as firm in the center as on the spinal surface, and presented much the same quality and consistency

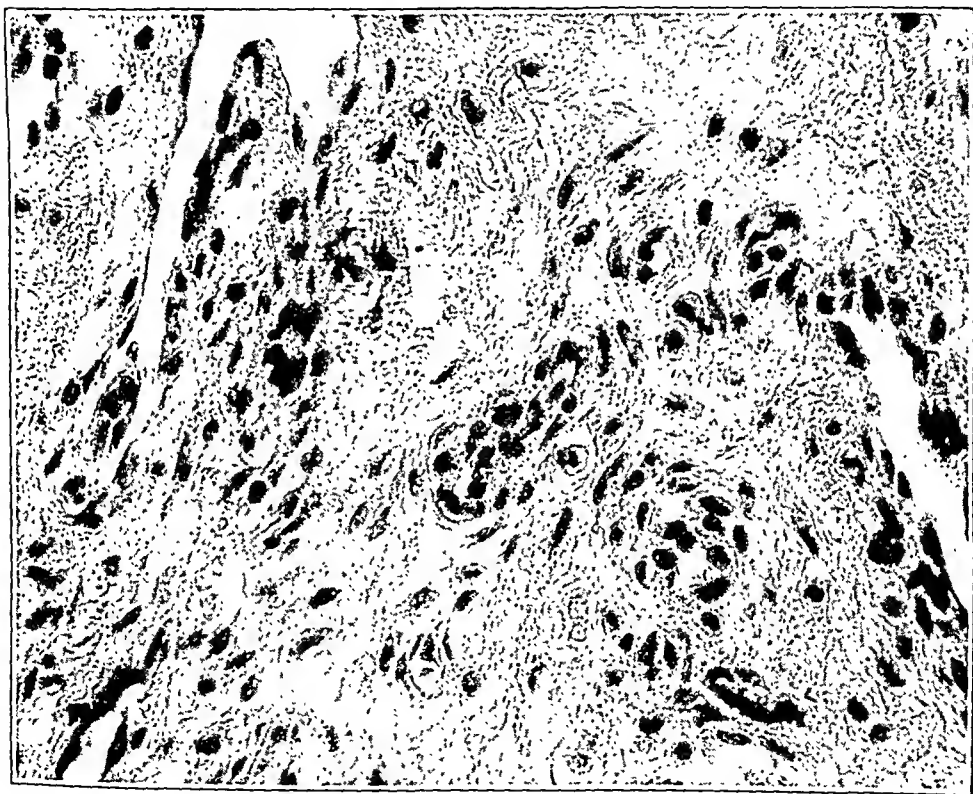


Fig. 8.—Photomicrograph of specimen of healed disk in the case of L. I. The block of new tissue was taken in the usual manner three months after thorough curettement had been done. The cavity was completely repaired with tough fibrocartilaginous scar tissue. Note the abundance of young fibrocartilage cells engaged in the process of repair.

as does cartilage. A block was removed for microscopic study. The latter showed the development of new fibrocartilaginous tissue, with invasion of many young cells (see figure 8).

The patient made an uneventful recovery from the operation and from the episode of acute pain low in the back. Follow-up letters were gratifying and, so far as I know, she has remained free of pain to the present time.

## VIII. ETIOLOGY

The consensus at present is that trauma plays the important role as a causal factor of herniating intervertebral disk. This concept has even given rise to the term "fractured disk." I should like to present considerable evidence, however, that trauma or injury of the back probably is not the initial cause of the changes in the disks that ultimately lead to herniation but only aggravates, hastens or precipitates the symptoms of an already existing degenerating and inadequate disk.

1. As brought out in a previous report,<sup>2</sup> about one fourth of the patients presenting the syndrome of herniating disk cannot recall an injury to the back of any consequence. The signs and symptoms develop gradually and are not associated with trauma. It is true that three fourths of the patients do recall one or more incidents of injury to the back and to one of which they often date the onset of the symptoms. Some of these injuries are severe, such as falling several feet in a sitting position. Many of the so-called injuries are trivial in respect to traumatic force such as that which occurs when one lifts a suitcase or bucket of water. The incidence, however, is one of real injury to the back of the patient, because the "catch," or "snap," that he experiences in the lower part of the back or the hip, which may also be associated with sciatic radiation, is accompanied with severe and excruciating pain.

The great majority of patients who date their severe pain to a relatively recent injury will, if questioned, give the histories of previous pain low in the back, weak back, stiff back and episodes of pain low in the back that have often been experienced for many years. If the disk has undergone advanced degeneration and the annulus fibrosus has become so thin as to be an inadequate capsule, it is obvious that a crushing force or strain may provoke one of three occurrences. The soft disk, being an inadequate joint, may allow a too severe pull or sprain of the ligaments, muscles and tendons about the lumbosacral region. This is accompanied with a sudden sickening and aching pain comparable to that of a sprained ankle. A second possibility is bulging, or herniation, of the disk capsule into the spinal canal, with consequent compression of a corresponding nerve root and with its attending symptoms, the severity of which depends on the degree of herniation. Third, the capsule may rupture and varying amounts of a sequestered nucleus pulposus be extruded. In such a case compression of the root is severe and unrelenting, and such patients are usually confined to bed until relieved by operation. Hence, it is perfectly reasonable to believe that trauma, mild or severe, may be only an aggravating factor to an existing pathologic condition.

2. When an injury to the back is severe enough to cause a break in continuity or dissolution of tissue, one sustains a subluxation or dislo-

cation of a joint or a fracture. So far as I can ascertain, a normal intervertebral disk is the last structure to suffer fracture or damage. It is the vertebral body that is fractured. I have never witnessed a fracture or rupture of a normal intervertebral disk due to the usual injury of the back. It would be most difficult to believe that the type of injury of the back under discussion could possibly cause a herniation or rupture or "fracture" of a normal intervertebral disk and, moreover, leave the bony spine intact. Saunders and Inman<sup>18</sup> gave a good account of the pathologic changes of the intervertebral disk. In respect to traumatic rupture, they made the following statements:

Traumatic rupture of the cartilage plate occurs in conjunction with compression fracture of the vertebral body, but it has been remarked how often the disk escapes injury even in the most severe lesions. . . . An important variety of trauma to the cartilage plate is that associated with marginal fracture of the vertebral body. These chip fractures are commonly anterior in position and are in themselves insignificant but, from roentgen evidence, are followed by collapse and thinning of the disk. . . .

We should like to emphasize that posterior herniations are in the great majority of instances evidence of general disk degeneration.

3. The changes which occur in a disk that has progressed to herniation are changes that develop slowly and undoubtedly require considerable time to reach the end stage. I have had experience with some patients in whom acute sciatica developed, the onset of which was one to two months previously and which was attributed to an injury of the back. There were no antecedent symptoms. At exploration, ruptured disks were found, the sequestered portion of the nucleus having been suddenly extruded into the spinal canal and accounting for the sudden, severe and unrelenting sciatic pain. In such a case, one is certainly tempted to view the lesion as a "fractured" disk which was sustained at the time of injury. Grossly and microscopically, however, it is obvious that the changes leading to the final stage had probably been progressing for years. Not only does the nucleus pulposus undergo the changes described, but it is necessary for the annulus fibrosus to degenerate if posterior herniation is to occur. When viewed in cross section, the annulus, posteriorly, is a laminated structure about  $\frac{1}{4}$  inch thick and having the toughness of leather. It is hardly reasonable to believe that nuclear material could be squeezed through such a structure unless the latter had in some place lost its integrity through degeneration. Studies of disks in various stages of degeneration reveal that the annulus does take part in the degeneration, loses its "onion peel" appearance and becomes so thin as to be incapable of retaining the nucleus even under normal stress. Such a process is obviously not a sudden one

18. Saunders, J. B. de C. M., and Inman, V. T.: Pathology of the Intervertebral Disk, *Arch. Surg.* **40**:389-416 (March) 1940.

and cannot be attributed to an incident of trauma to the back which dates the onset of the symptoms of herniating disk. If one subscribes to trauma as the cause, one can only propose that some previous injury set into progress the changes in the disk described; however, this particular injury would not necessarily date the onset of the syndrome of the herniating disk.

4. Eighty-seven to 98 per cent of the herniating disks occur below the fourth or fifth lumbar vertebrae. This is an outstanding observation and one which has not been satisfactorily explained. Since the consensus favors trauma as the etiologic factor in pathologic changes in disks, it is only consistent to propose that stress and strain are greater at the lower two lumbar segments. This seems to be stretching a point rather far when one recognizes how sharp is the demarcation between the lower two lumbar disks and all those above in respect to incidence of herniation. Furthermore, it is uncommon to sustain compression fractures of the fourth and fifth lumbar vertebrae. Fractures are usually of the first and second vertebrae or higher, an indication in itself that the greatest flexion compressive strain is not at the fourth and fifth lumbar segments.

5. Embryologically, the nucleus pulposus is derived from a "pinched off" remnant of the notochord, and in the growth and development of these structures many displacements and abnormalities occur, such, for example, as Schmorl's node and spondylolisthesis.<sup>19</sup> If a degenerating intervertebral disk has a congenital or developmental basis, it is not unreasonable to expect the greatest incidence to be at the caudal end of the notochord. Note the defect in the fifth lumbar disk in figure 3. It is such that the nucleus has been divided into two parts.

In many instances of herniating disk one will find only a pea-sized herniation laterally placed. One finds that only a small part of the nucleus pulposus has sequestered and rests in a walled-off pocket. The remainder of the nucleus is apparently normal. Furthermore, others, as well as I, have encountered herniating disks in patients whose ages ranged from 17 to 22 years who had no history of significant trauma to the back.

6. Inflammation has been kept in mind as a possible etiologic factor, and the beefy red appearance of some degenerating disks strongly suggests an inflammatory change. However, I have never been able to demonstrate the elements of the inflammation microscopically.

Therefore, when the three major factors in respect to the causation of degenerating and herniating disk are considered, namely, trauma, inflammation and faulty development, the evidence certainly promotes

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19. Ehrenhaft, J. L.: Development of the Vertebral Column as Related to Certain Congenital and Pathological Changes, *Surg., Gynec. & Obst.* **76**:282-292 (March) 1943.

a strong consideration that favors faulty development as the primary causal factor. If faulty development is an important factor, the nature of the pathologic changes still, nevertheless, remains unexplained. Deficient blood supply is a possibility that might at first seem to merit consideration, but Keyes and Compere<sup>8</sup> stated that the intervertebral disk contains neither blood vessels nor nerves and that its nutrition is supplied entirely by the lymph stream. These authors found congenital imperfections in the cartilage plates and gave evidence to show that splits and tears may be caused by trauma. They proposed that these defects may lead to gradual dehydration of the nucleus and lessen the resiliency and efficiency of the disk. This concept offers a possible explanation for degeneration of disks as a result of congenital imperfections and also as a result of trauma. Just how important a role is played by each is not yet clearly understood.

At present, all indications lead to a conviction that if one has intervertebral disks of perfectly normal integrity developmentally one will not be subject to herniation of a disk regardless of hard labor or injury to the back. The idea that a degenerating or herniating disk may be due to faulty development is not entirely new. For example, Echols<sup>20</sup> stated, "The fact that multiple ruptured disks are often found in cadavers suggests predisposing factors, such as degenerations or congenital imperfections of the disks."

The inadvertent passage of a spinal puncture needle into an intervertebral disk has been cited as a cause for degeneration of a disk.<sup>21</sup>

I do not feel that the evidence as presented in reports of cases has been conclusive. The sequelae of the type of trauma that has been inflicted on the disks of laboratory animals<sup>8</sup> are an entirely different matter and are not comparable to the type of trauma incident to a needle puncture in human beings. I have passed a spinal needle through the annulus a number of times when a disk was exposed at operation. The puncture wound closed tightly when the needle was withdrawn, and not a particle of nucleus tended to extrude. The wounds appeared so benign that it would require a great stretch of the imagination to believe that they might be cause for herniation. If at all likely, it would surely require a long time for the usual degenerative process to obtain. It is more likely that such a puncture wound would heal forthwith by first intention. Moreover, spinal punctures are commonly done and usually at a point higher than the common location of herniating disks. By far

20. Echols, D. H.: The Neurologic Aspects of Low Back Pain and Sciatica, *J. A. M. A.* **125**:416-420 (June 10) 1944.

21. Downing, F. H.: Collapse of Intervertebral Disc Following Spinal Puncture, *U. S. Nav. M. Bull.* **43**:666-673 (Oct.) 1944. Gellman, M.: Injury to Intervertebral Discs During Spinal Puncture, *J. Bone & Joint Surg.* **22**:980-985 (Oct.) 1940.



the majority of patients who present herniating disks have never had spinal punctures previous to the onset of symptoms.

In any case, before it is concluded that a spinal needle might be cause for degeneration and possibly herniation of disks, reports should be accompanied with incontrovertible proof, not only because of scientific reasons but because of the serious import and medicolegal implications.

#### IX. TERMINOLOGY

*A. According to the Degree of Degeneration.*—1. Grade 1 Degeneration: Grade 1 degeneration is an early stage of degeneration without herniation. The annulus fibrosus is eroded, weakened and thin enough to allow penetration of a bayonet forceps with moderate pressure, but it is not of "paper thinness." Macroscopic examination reveals definite degenerative changes in the nucleus pulposus, consisting in dehydration, partial sequestration and often a red, "inflamed," appearance. The specimen on the left in figure 6, taken from the fourth lumbar vertebra, is classified as grade 1 degeneration.

2. Grade 2 Degeneration: Grade 2 degeneration is an advanced stage of degeneration without herniation. In this case the annulus fibrosus is thin and has little resistance to pressure. A part or all of its posterior surface may be punctured with the tip of a bayonet tissue forceps or similar instrument, with no more resistance than a sheet of paper. The point of the forceps appears to sink into a soft nucleus without substance. The nucleus may be "mushy," or it may appear desiccated, stringy and fibrous. One has the impression that such a disk is on the verge of herniation.

The specimen on the right in figure 6, taken from the fifth lumbar vertebra, is an example of grade 2 degeneration, because of the almost complete erosion of the annulus in one location.

3. Grade 3 Degeneration: Grade 3 degeneration is an advanced stage of degeneration in which herniation, or rupture, of the annulus occurs. Figures 1, 4 and 7 illustrate grade 3 degeneration.

*B. Extended Classification.*—1. Herniating Intervertebral Disk: Any pathologic protrusion of a disk is classified as herniating intervertebral disk. The herniation is usually on only one side of the spinal canal and is thus designated as being on the right or on the left.

In about 7 per cent of the cases, the herniation extends clear across the spinal canal. These herniations are designated bilateral. They are often associated with symptoms and signs of compression of the nerve root on both sides.

In a small percentage of cases the herniation will be centrally placed and without sufficient protrusion laterally under the nerve roots to cause compression of the latter. Such an example is classified as central

herniation. These cases may be confusing when symptoms and signs are being evaluated. The patient usually presents the syndrome of degenerating disk without herniation. In a number of patients for whom the diagnosis of degenerating disk was made and in whom herniation was not suspected, this type of central herniation was unexpectedly found.

2. Ruptured Intervertebral Disk: If the annulus fibrosus is ruptured and a portion or all of the sequestering nucleus is protruding through it, the disk is designated as ruptured. If the nucleus is completely sequestered and can be pulled away in one piece, it is referred to as a ripe disk. If it is not completely sequestered and it is necessary to use the curet, the disk is referred to as being green. It would naturally follow that all pathologic disks in which the nucleus pulposus is not completely sequestered are green disks.

3. Pocketed Sequestration: If only a portion of the nucleus has undergone degeneration and sequestration and the rest of the disk appears normal, the lesion is called a pocketed, or partial, herniation, or sequestration. As already pointed out, patients who present this type of herniation are likely to give little or no history of pain low in the back. The symptoms and signs are related to only compression of a nerve root (see report of case of E. C., under section on operation).

4. Dissecting Herniation: In a small percentage of cases (2 to 3 per cent) in my experience, a sequestered nucleus, instead of rupturing through the annulus, will dissect and inspissate itself upward or downward under the disk capsule (see report of the case of E. C., under section on operation). This is referred to as the dissecting type. The major portion or all of the extruded nucleus might be overlooked, especially if the operative exposure is not adequate.

5. Calcified or Ossified Herniation: Herniations that have been present for many years may have become surrounded by a lip, or cone, of bone. The sequestered nucleus itself does not calcify, but spurs of bone from the margins of the vertebrae extend into the spinal canal above and below the herniation. The spurs may approach each other so closely as to almost encase the herniation. Until the spurs are chiseled or rongeured away, one may find it difficult to insert a curet between the vertebrae. The spurs contribute to the compression of adjacent nerve roots and should be removed. They may present in the lateral roentgenogram of the lumbosacral portion of the spine. An example of spur formation about a bulging annulus is demonstrated in figure 2, although the lesion was not a degenerating-herniating disk in the strict pathologic sense.

6. Herniation Within the Intervertebral Canal: The intervertebral canals are the channels through which the spinal nerves make their

exit from the spinal canal. In strict anatomic nomenclature they are referred to as intervertebral foramens, but the channels are of sufficient length that they might also be termed canals, and it is more appropriate in relation to this presentation that they be visualized as canals. An intervertebral canal is bounded superiorly and posteriorly by a pedicle and an inferior articular process respectively of one vertebra. It is bounded anteriorly by the body of that vertebra. The inferior boundary is formed partly by a superior articular process of the next lower vertebra and partly by the intervertebral disk between the two vertebrae.

Herniation strictly confined within the limits of the intervertebral canal deserves considerable attention. It may be rare, but it also may be present when the exploration has been considered noncontributory, because it has not been customary to explore the intervertebral canal. Inasmuch as this type of herniation relates to location or position of the herniation, it might well have been included under the heading herniating intervertebral disk, but I have purposely classified it as a separate entity to draw special attention to it. It is an obscure lesion and may be easily overlooked. At present its incidence cannot be evaluated, but I can see no reason from anatomic or pathologic standpoints why herniation could not occur within the intervertebral canal just as easily and as often as it does into the spinal canal. The fact that the majority of intraspinal herniations are laterally placed bears out this suspicion. Indeed, one should explore these lateral herniations carefully to make sure that they do not extend into the intervertebral canal. If such a herniation does extend into the canal, it would compress the nerve that is just cephalic to the one that is compressed by the intraspinal portion of the herniation.

I have recently uncovered three striking examples of ruptured disks with extrusion of nuclear material strictly confined to the intervertebral canal. The cases are described under the section on operation.

*Recurrent Herniations.*—I have encountered only 2 cases of undisputed recurrent herniations. In 1 patient a large right-sided herniation developed three months after a left-sided herniation was curetted away. Herniation was not present on the right at the first operation. At that time, curettement of the nucleus was not so thorough as is done now.

The second patient suffered a sudden extrusion of a completely sequestered nucleus six years following the original operation. Six years ago a herniated disk was partially curetted, with complete relief of symptoms at that time.

Thorough curettement of the pathologic disk, while important in the consideration of possible recurrence, has not been emphasized so much in the interests of possible further herniation or recurrence as it has been in the idea of attainment of as complete a fibrocartilaginous fusion as possible. I do not believe that degenerating and sequestering

nuclear material will incorporate itself satisfactorily into the development of the "fusion scar."

#### X. THE OPERATION

*Indications.*—The diagnosis of herniating, or ruptured, intervertebral disk in its usual location (below the fourth or fifth lumbar spaces or both) can be made with great accuracy from the history and clinical findings. In fact, experience in the past few years has taught that chronicity of symptoms, unilateral distribution and typical sciatic radiation of pain warrants the diagnosis of herniating intervertebral disk. Unless there is something unusual about the history and findings, myelograms with air and iodized poppyseed oil are unnecessary and might be even misleading if normal. Myelography with air or iodized poppyseed oil would be of no avail in the diagnosis of degenerating disk which has not herniated. This diagnosis must be made on the history and examination and chiefly the history. The myelogram would not indicate a herniation confined to an intervertebral canal.

Steindler's test with procaine hydrochloride may be used to advantage in differentiating reflex sciatic from radiating sciatic pain. Since it has been postulated that reflex pain down the lower extremity is not due to compression of a root but is reflected from a painful myofascial locus, the pain can be temporarily expunged by locally anesthetizing the myofascial locus (trigger zone). Not only is reflex pain and tenderness of the trigger zone relieved, but straight leg raising can be performed without pain. One may deduce from such positive results that the symptoms and signs may be due to a degenerating disk but not to a herniating disk. This situation should be made known to the patient because if he elects conservative treatment for a time it would not be so ill chosen as it would if he had a herniating disk. If the disk is herniating, the radiating sciatic pain would be due to compression of a root and would not be relieved by injection of procaine hydrochloride. In this case surgical treatment could be advised without equivocation. In cases, therefore, in which it is doubtful whether the degenerating disk has herniated or not, the test with procaine hydrochloride may provide the answer and fortify the surgeon for a more accurate approach to the problem and advice to the patient.

In an operative experience with 800 cases of herniating intervertebral disk and 42 cases of degenerating disk without herniation, the best results have been obtained with a thorough and complete operation which is outlined in the following paragraphs.

*Procedure.*—Since about 6 per cent of patients will have pathologic changes in the disks at both the fourth and the fifth lumbar spaces, it is advisable to explore both disks routinely. This 6 per cent applies to actual herniating disks at both places. A group of patients will present herniating disks at one of the two locations and degenerating disks at

the other. Another group will present degenerating disks at both places. No doubt many of the unsatisfactory operative results can be explained by the fact that one of these pathologic disks was unexplored and untreated.

The spinous processes of both the fourth and the fifth lumbar vertebra are removed. After the erector spinae muscles have been stripped from the spinous processes, one may grasp the latter with an instrument and determine the degree of fixation of the vertebra at that segment. When a degenerating disk is present, it is rather common to find that the adjacent vertebrae are not normally and solidly fixed. The laminal arches are scraped widely. The ligamentum flavum is then dissected from its cephalic laminal arch by a semicutting instrument. A tonsil dissector is a suitable instrument. The lower third of the fourth and fifth lumbar arches is rongeured away, the removal being carried equally wide on the two sides. The ligamentum flavum is then split in the midline to the dura. A blunt instrument is inserted between the ligament and the dura and held by an assistant while the ligament is removed as completely as possible on both sides. Finger palpation for the herniated disk is then done, but regardless of the impression the nerve root is retracted mesially and the disk is inspected. If the disk is herniated, or ruptured, it is easily disclosed by palpation or inspection. The first observation is that the nerve root is displaced posteriorly and comes into view quickly in the process of dissection. By means of a curved, blunt instrument the root is separated from the underlying lump and retracted mesially. This procedure may be difficult at times and requires care and patience because of an unusual adherence of dura to the herniated disk. If the nucleus pulposus has ruptured and is completely sequestered (in which case it is referred to as a "ripe" disk), it can be grasped with a tissue forceps or hemostat and pulled in toto from its bed, and further operation on such a disk is unnecessary. If it can be established that a sequestered portion of nucleus is "pocketed" and encased in a well formed capsule and the remainder of the disk feels of normal integrity, the latter is not incised or further curetted. If the annulus is or is not ruptured and the entire disk (nucleus and annulus) is soft and undergoing degeneration, then the annulus should be cut away as widely as possible with a sharp stab blade, much as one would plug a watermelon. The nucleus is then curetted away as thoroughly as possible. The nerve root on the opposite side is then retracted and the remainder of the annulus fibrosus cut away. All the remaining nucleus is curetted away. In making the exposure preparatory to retraction of the nerve root, one should dissect and remove the ligamentum flavum that lines the lateral wall of the spinal canal and rongeur bone as widely as possible without destroying the articular facets. This gives better exposure and thorough decompression and helps to obviate injury to the nerve root.

If the disk is not bulging or herniated, the operator should test the integrity of the capsule by trying to force the tip of his bayonet forceps through it. With reasonable force he will not be able to penetrate the normal capsule. If the capsule is thin and degenerated, the forceps will penetrate it and sink into an obviously soft nucleus.<sup>22</sup> Such a disk is curetted bilaterally as already described.

The wound is closed with tiers of interrupted silk, and a Penrose drain is left in place to be removed in twenty-four hours.

If it is necessary to treat only one disk, the patient is required to remain in bed two weeks. If it is necessary to curet two disks, he is required to remain in bed three weeks. This time is arbitrary but is certainly the minimum time required to assure that proper healing is well under way.

I have entertained the idea of placing fragments of bone in the disk cavity after the nucleus pulposus has been curetted away. The purpose is to stimulate actual bony fusion of the vertebrae if possible. This has been done in 4 cases, but sufficient time has not elapsed to draw conclusions. In each case, a whole spinous process was scraped of all tissue except periosteum. It was then crushed in several places and wedged into the intervertebral cavity. In a roentgenologic check-up of 1 patient three months after operation there was no evidence whatever of beginning ossification. If anything, it appeared that the fragment of bone was undergoing absorption. However, the idea is worthy of consideration, and more information will be forthcoming.

The postoperative course in my experience has not yet indicated the necessity of bone grafting as an additional procedure. I feel that the application of loose bone chips in the wound has little value in respect to the purpose intended and does add to the hazards of infection. I reexplored a patient recently in whose wound bone chips and fragments had been placed six months previously. The chips were resting as foreign bodies and in no way had aided in the solidification of the lumbosacral joint. I have felt that the application of casts has been rarely necessary. The lumbosacral portion of the spine appears to be sufficiently immobile of itself, so that two to three weeks in bed on a

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22. Dandy (Concealed Ruptured Intervertebral Disks: A Plea for the Elimination of Contrast Mediums in Diagnosis, *J. A. M. A.* **117**:821-823 [Sept. 6] 1941.) has referred to this entity as a "concealed disk" but implied that it causes the same symptoms and signs as a herniated disk. This is true if the disk bulges enough under stress to compress the adjacent nerve root. The purpose of the present report is to point out that such a pathologic disk can be the cause of chronic pain low in the back without bulging and without compression of the root and can be adequately treated by operation. In a recent paper (Recent Advances in the Treatment of Ruptured [Lumbar] Intervertebral Disks, *Ann. Surg.* **118**: 639-646 [Oct.] 1943) Dandy has also stated the conviction that a "concealed disk" can be cause for pain low in the back without sciatic radiation.

properly fixed mattress and another one to two months of reasonable care will establish proper healing. Moreover, since the objective is the development of a fibrocartilaginous disk or scar in the place of the pathologic disk, the problem is somewhat different from that involved in the healing of a fracture of bone. In the event of extensive operation, such that the bony integrity of the spine is substantially weakened, bone grafting as an adjunct may become advisable. With the discovery of herniations in the intervertebral canals and other remote loci the scope of surgical treatment in this entity is broadened, and in some cases the proper and necessary operation involved may warrant tibial bone grafting or casting. It is not my purpose at this time to propose hard and fast rules concerning the principle of bone grafting as an adjunct procedure and certainly not to renounce it completely. In my experience, results have not indicated the necessity of supplemental grafting in the cases in which one disk has been curetted and the articular processes of the vertebrae have not been interrupted. The accessory procedure should not be done indiscriminately without consideration of the substantial increase in the magnitude of the operation, the element of time and the cost to the patient. Insofar as the laminectomy alone is concerned, the complete removal of as many as six or seven arches in numerous patients for various neurosurgical procedures has not been followed by evidence of instability of the spine, and bone grafting would appear superfluous. I feel that the matter is an open question and that each case should be determined on its own merits.

I feel that too much emphasis cannot be placed on the fact that small herniations, and particularly small extrusions of nuclear material, may be situated so far laterally in the spinal canal that they may be overlooked easily by palpation and may not be disclosed to inspection until the nerve root has been reflected mesially and down to its entry into the intervertebral canal. This type of exploration will necessitate removal of at least the cephalic half or perhaps all of a laminal arch laterally. The "dissecting type" of herniation may present the sequestered nuclear tissue in this way in remote and obscure places and necessitate an extended thorough exploration to disclose and remove it. The following 2 cases illustrate the point particularly well.

E. C., a white man aged 67 years, was admitted to St. Joseph's Hospital on Oct. 28, 1945. He was a carpenter by trade. Three months before, at a time when he was physically at rest and not straining his back, he rather suddenly began to experience pain which radiated throughout the sciatic distribution on the left side only. He located the pain as coursing from a spot to the left of the sacrum, down the posterior aspect of the thigh and through the calf and involving the mesial half of the left foot and toes. He explicitly denied any history of pain low in the back either before or after the onset of sciatic pain. This was also his first experience of sciatic pain. The pain rapidly became so severe that he remained confined to bed until relieved by operation. All the signs

of compression of a nerve root were present except for the fact that the achilles tendon reflexes were equal.

At operation, a limited sequestration was disclosed at the fourth lumbar vertebra on the left. The annulus was ruptured, and an amount of sequestered nucleus about the size of the rubber on a lead pencil was protruding through the defect and severely compressing the fifth lumbar root. The lesion was not disclosed until the cephalic half of the fifth laminal arch on the left was removed and the fifth lumbar root reflected mesially. The location of the rupture is shown in figure 9. It might have been easily overlooked had an extended search not been made. It would be a tragic circumstance to close a wound without finding the existing herniating disk that is responsible for the patient's complaint. Not only would the patient be unrelieved, but the diagnosis would remain obscure and one would be reluctant to reexplore. If the diagnosis of herniating disk is made, the surgeon should thoroughly explore every possible locus of herniation before pronouncing the exploration noncontributory.

The case just described illustrated clearly some other notable factors related to herniating disk. First, the sequestration was limited and was of a pocketed type, while the remainder of the disk was of good integrity. The patient experienced no pain, therefore, until the portion of sequestered nucleus was extruded and impinged on the adjacent nerve root. He denied pain low in the back and described only sciatic pain. The syndrome was an acute one, and he was compelled to remain in bed, with unremitting pain from its onset until relieved by operation. The fact that the pathologic changes and their attending symptoms presented at the age of 67 for the first time is interesting and might favor trauma or wear and tear as the causal factor for the localized degeneration.

J. F., a white man aged 39 years, was admitted to St. Joseph's Hospital on Jan. 26, 1946. He had complained of pain low in the back for two years. Pain radiating in the sciatic distribution on the left side had its first onset spontaneously only two weeks before. Pain and paresthesia were referred to the small toe on the left as well as to the posterior part of the thigh and lateral aspect of the leg. Coughing aggravated the pain.

On examination all the findings related to herniating disk as described in this paper were present, including positive results from a straight leg raising test on the left and an absence of ankle reflex on the left. The knee reflexes were equal and active.

*Operation.*—On the definite diagnosis of herniating intervertebral disk a laminectomy was performed on Jan. 27, 1946. The fourth and fifth lumbar disks were explored thoroughly in the usual manner, but no herniation was disclosed at first in the spinal canal. The intervertebral canals at the fourth and fifth lumbar disks allowed the easy passage of a grooved director through them, so that it did not seem likely that there was a herniation in one of these canals. The findings on examination certainly were not those of herniation at a higher level. In fact, they rather definitely indicated an involvement of the left first sacral root. The usual inspection and mesial retraction of the first sacral root on each side revealed nothing abnormal, and, moreover, the annulus at both the fourth and the fifth lumbar vertebrae was firm and of normal toughness. An instrument passed upward to the second and third lumbar vertebrae extradurally met with no obstruction. The situation was indeed incredible. Since there



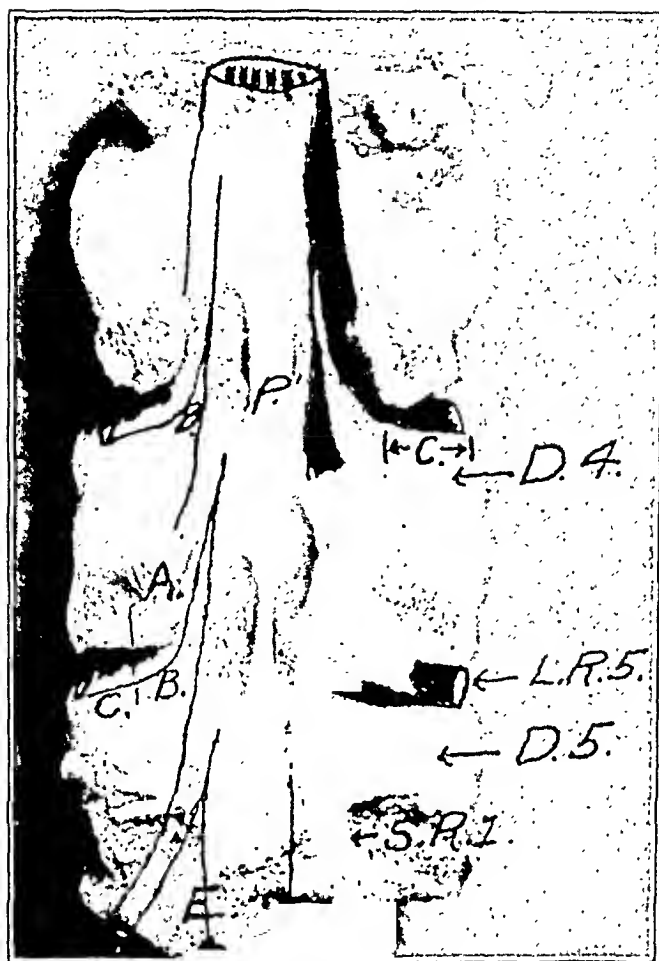


Fig. 9.—Semidiagrammatic sketch to illustrate unusual loci for herniations of disks. The photograph was taken of the specimen used in figure 3. The laminal arches and ligamenta flava have been largely removed to expose the spinal canal. The dura and nerve roots have been drawn in.

The limited or pocketed nuclear sequestration described in the case of E. C. had dissected downward under the annulus of the fourth dorsal space and presented at point *A*, compressing the fifth lumbar root on the left. Such sequestrations may dissect upward and present at point *B*. The sequestrated nucleus in the case of J. F. presented at locus *E* on the body of the first sacral vertebra. These limited lesions may be overlooked if exploration is not thorough. Inasmuch as the nerve root is fixed and contained in a limited space at these loci, a small amount of extruded nucleus will compress it severely.

Experience with lesions such as these raised the question of the possibility of herniations, or ruptured sequestrations, within the confines of the intervertebral canal, such as at locus *C*. The locus marked *C* at the fourth lumbar disk on the right represents the location of the rupture in the case of J. W. The rupture and nuclear extrusion were strictly confined within the intervertebral canal.

Note how the posterior longitudinal ligament (*P.*) bridges over the vertebral body and fans out over the intervertebral disk.

*D.4* and *D.5* indicate the fourth and fifth lumbar intervertebral disks, the fifth being the last, since there are no intervertebral disks between the sacral segments. *L.R.5* indicates the fifth lumbar nerve root and *S.R.1* the first sacral root.

could be little question about involvement of the first sacral root, the laminal arch of the first sacral vertebra was removed and an amazingly large extruded nucleus presented. The sequestered nuclear material had been extruded from a pocket in the center of midsagittal plane of the fifth lumbar disk and had dissected caudalward under the annulus to present over the body of the first sacral vertebra. The nucleus rested in a shallow excavation on the body of the first sacral vertebra and compressed the first sacral root on the left at the place where it entered the first sacral canal (see figure 9, locus *E*). The extruded nucleus was easily pulled away in one piece. The lesion might have been easily missed and the exploration thought to have been complete.

In figure 9 I have marked loci where obscure lateral or dissecting herniations may be found.

*Extended Exploration for Herniation in an Intervertebral Canal.*—This subject is purposely treated under a special heading in order to add the special emphasis that it merits. After I had been confronted with herniations in an extreme lateral position, the question arose concerning the possibility of a pocketed type of sequestration and rupture within an intervertebral canal itself. This should be given consideration when the diagnosis of compression of a root seems clear and no herniation is found within the spinal canal.

The first patient (J. W., to be described) in whom I disclosed a definite herniation of this type was operated on in December 1945. In the following month, being fortified sufficiently with the newly gained knowledge to carry my exploration into the intervertebral canals, I encountered 2 more striking examples of cases of this kind. In 1 of the patients a partially extruded nucleus presented at both the fourth and the fifth lumbar intervertebral canals on the left. In these 2 additional cases, those of A. H. and W. Van C., an intraspinal exploration, however thorough, would have completely failed to disclose the pathologic change and causal factor for the sciatic pain. It was not until the intervertebral canals themselves were exposed that the lesion presented itself. Moreover, the spinal decompression alone could not have conceivably relieved the compression of the nerve root. After the experience with these 3 patients I am convinced of the strong probability that this heretofore obscure type of herniation yet resides unrelieved in some patients who have had so-called negative explorations. In the past three years I have operated on 2 patients who presented definite herniating disk syndromes with all the positive signs of compression of nerve roots, including an absence of the achilles tendon reflex on the painful side. A thorough intraspinal exploration failed to disclose a herniation or satisfactory explanation for the symptoms and signs of the compression of the roots. The patients were not relieved of their complaints and are being recalled for the purpose of the exploration of the intervertebral canal or canals in question. At the present time the following pertinent and informative statements may be made in reference to the herniation of the intervertebral canal.

1. A herniation, or rupture, can occur only in the intervertebral canal that is cephalic to the pathologic disk. The intervertebral disk forms the caudal boundary of the pair of intervertebral canals that lies just cephalic to the disk, but this same disk is not related to the intervertebral canals that lie caudal to it. Hence, in a normal anatomic situation the first sacral nerve root is not subject to compression by a herniation confined in an intervertebral canal.

2. A herniation confined within an intervertebral canal will compress the nerve root in that canal. Thus a herniation of the intervertebral canal from the fifth lumbar disk will compress the fifth lumbar nerve root. One from the fourth lumbar disk will compress the fourth lumbar root and may cause signs that would lead to a suspicion of an intraspinal herniation at the third lumbar disk, namely, hypalgesia in the fourth lumbar distribution and a diminished patellar reflex, while the achilles tendon reflexes remain equal. If a herniation, or rupture, is intraspinal and extends also into the adjacent intervertebral canal, say at the fourth lumbar space, it may compress both the fourth and the fifth lumbar root and thereby cause diminished patellar and achilles tendon reflexes on one side, with noticeable weakness of the ankle. Hence, if signs of involvement of the fourth lumbar root are present, it does not necessarily follow that a herniation must be as high as the third lumbar disk.

3. The fact that the intraspinal aspect of the annulus fibrosus proves to be of normal firmness and integrity does not rule out the possibility of a herniation in the intervertebral canals just above it. In all 3 of the cases described in the following material the intraspinal aspect of the pathologic disks appeared normal, and the annulus in each instance was of normal toughness. It so happened that in these 3 cases the nuclear sequestration was of a partial or pocketed type, and hence no clue to the likelihood of herniation in the intervertebral canal was provided by a general degeneration of the disks. It is, of course, conceivable that in other cases the defective disk will betray itself by a more extensive degeneration and annular erosion in its intraspinal aspect.

4. At present I feel that one can deduce some information relative to the possible presence of a herniation in an intervertebral canal by attempting to pass a suitable instrument through the latter. Such an instrument should be devised exclusively for this purpose and be of such a caliber as to pass through the unobstructed canal with relative ease. Thus far a grooved director, properly bent, serves the purpose reasonably well. In patients A. H. and W. Van C., described later, this instrument was passed with ease through normal canals and met with definite obstruction where herniations were present.

5. The intervertebral canal may be unroofed and exposed partly with suitable rongeurs and partly with chisel and mallet. Thus far I

have found it necessary and advisable to remove the inferior articular process or mesial facet of the vertebra, the canal of which is being explored.

6. Myelography with iodized poppyseed oil, Pantopaque or air would obviously be of no diagnostic value in the visualization of the presence of herniation of an intervertebral canal.

7. Under the section devoted to the roentgenogram; some comments were made concerning the narrowed or collapsed disk. Two cases were cited in which the roentgenograms revealed completely collapsed disks, but no intraspinal herniation was found at exploration. The patients were relieved by decompression of the corresponding intervertebral canals. At that time my decompression of the intervertebral canals was not complete. It consisted largely in widening of the intraspinal orifice of the canal and may not have been of sufficient scope to have brought a possible intracanalicular herniation into view, especially since my attention was not directed to a possible herniation at this locus. Hence, in such cases the possibility of herniation of an intervertebral canal has not been entirely cleared. Knowledge concerning these matters is still in the formative stage.

#### REPORTS OF CASES OF HERNIATIONS OF THE INTERVERTEBRAL CANAL

J. W., a white man aged 62 years, was admitted to St. Joseph's Hospital on Dec. 13, 1945. He described pain low in the back with typical sciatic radiation on the right, to and including the foot. He dated the onset a year before, following a strain on the back while he was roping a steer. He presented all the significant symptoms and signs of herniated disk but also presented a diminished knee jerk on the right. The roentgenogram showed rather narrow intervertebral spaces but otherwise nothing of special note.

A laminectomy was performed on Dec. 14, 1945. The annuli at the fourth and fifth lumbar disks were bulging into the spinal canal somewhat but were firm and of normal integrity and did not appear to account for the symptoms. While the fourth lumbar disk on the right was explored, a bit of nuclear material could be seen in the entrance of the adjacent intervertebral canal. Ultimately, that entire canal was opened, and a surprising amount of sequestered nucleus was found to be jammed into the canal, severely compressing the fourth lumbar root (see figure 9, locus C, at the fourth lumbar disk on the right, and see figure 10). The portion of the annulus which forms the inferior boundary of the intervertebral canal was ruptured, but the rupture did not extend into the spinal canal.

A. H., a white man aged 56 years, was admitted to St. Joseph's Hospital on Jan. 17, 1946. He had experienced some pain off and on in the sciatic distribution on the left for about twenty years. It became severe rather suddenly about eight years before, when he was reaching for a high shelf. He traced the course of the pain from a point to the left of the sacrum down the posterior aspect of the thigh. Pain was absent in the knee but was felt in the lateral aspect of the leg, the heel and across the top of the foot. He had never sensed pain in the right lower extremity. Pain on the left was aggravated by coughing and sneezing. For

years he had had considerable difficulty in resting at night because of the pain. Getting on his feet in the morning was an ordeal, and of late moderate activity had caused the pain to become intolerable. Function of the bowels and bladder was unimpaired.

The significant findings on examination were as follows: There was almost no lordotic curvature of the lumbar portion of the spine, but the latter presented a mild scoliosis to the left. The erector spinae muscles were extremely spastic on both sides. Forward bending to about 50 per cent of the normal maximum excited sciatic pain on the left. Patrick's maneuver caused no pain on either side, but straight leg raising was painful on the left. Moderate pressure over the spine of the fifth lumbar vertebra and over the left loin was uncomfortable, and the region of the sciatic nerve in the left thigh and the left calf was tender compared with those regions on the right side. There was a definite hypalgesia in the fifth lumbar distribution on the left. The patellar tendon reflexes were equal and

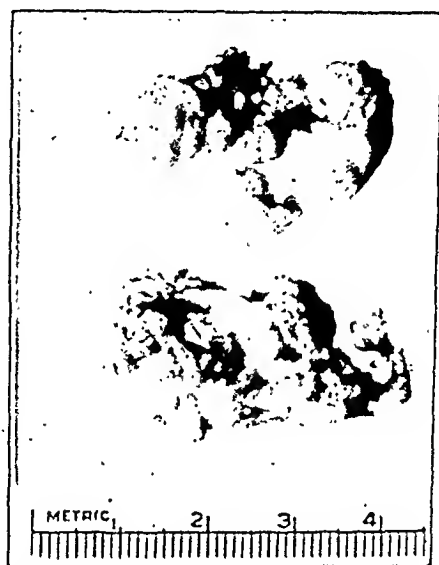


Fig. 10.—Photograph of sequestered nuclear material removed from the fourth lumbar disk in the case of J. W. The rupture of the annulus and nuclear extrusion were strictly confined within the limits of the intervertebral canal on the right (see figure 9). The upper piece of tissue was completely sequestered and jammed into the intervertebral canal, severely compressing the fourth lumbar root in the canal. The pieces of tissue in the lower half of the photograph were removed from a pocket within the disk.

This finding introduces a new possible location for herniation and ruptured disks, which to my knowledge has not been heretofore given attention. Such an obscure lesion may account for the persistence of symptoms after so-called negative explorations.

active, but the achilles tendon reflex was absent on the left. The abdominal, cremasteric and plantar reflexes were normal.

Roentgenograms of the lumbosacral portion of the spine revealed arthritic spurs on the margins of several lumbar vertebrae. The lumbosacral articulation in particular showed pronounced hypertrophic arthritis, with condensation of the opposing surfaces of the vertebra and the sacrum. The lumbosacral joint space was abnormally narrow. The sacroiliac articulation on the right showed hypertrophic arthritis in its lower aspect, with narrowing of the joint space and condensation of the opposing surfaces.

(NOTE: As pointed out in the chapter on the roentgenogram, it is not inconceivable that spurs and condensations about the low lumbar, lumbosacral and sacropelvic joints could be reactions to excessive strains and stresses that are themselves attributable to pathologic changes of the intervertebral disk and weakness.)

A definite diagnosis of herniating intervertebral disk was made.

*Operation.*—On Jan. 18, 1946, with the patient under anesthesia induced with tribromoethanol, the fourth and fifth lumbar intervertebral disks were explored in the usual manner. Pocketed sequestrations of nuclear tissue were found in the intervertebral canals at both the fourth and fifth lumbar disks on the left. The ruptures were confined within the limits of the intervertebral canals, and sequestered nuclear tissue was jammed against the fourth and the fifth lumbar roots in their respective canals. Both canals were completely exposed by removal of the inferior articular processes of the fourth and fifth lumbar vertebrae that form the dorsal boundaries of the canals.

The wound was closed as heretofore described without bone graft or application of a cast. After this amount of operation it is at present felt that the patient should remain in bed for three weeks. The necessity of grafting or casting is at present an open question. The patient sensed immediate relief of his acute pain on awakening from the anesthesia and at the present writing is up and about, with no significant complaints.

W. Van C., a white man aged 37 years, was admitted to Mercy Hospital, Denver, on Jan. 27, 1946. He had complained of pain low in the back for six years. One year before pain began to radiate down the left sciatic distribution, associated with a numb feeling in the left leg. There was no pain referred to the right lower extremity. Coughing and sneezing aggravated the pain, and pain in the left hip was aggravated at the time of bowel movement. For the past two weeks he had been confined to bed with acutely severe sciatic pain, which followed some hard work in the cornfields.

On examination the patient presented all the positive signs as outlined in this paper as related to herniating disk except for the following unusual ones: There was hypalgesia in the fourth lumbar distribution on the left, and the left knee, or patellar, reflex was definitely diminished. The achilles reflexes were equal.

*Operation.*—Because of the findings on examination, the third, fourth and fifth lumbar disks were examined. There was a partial degeneration of the nucleus and annulus of the third disk on the left, such that the annulus was almost completely eroded in an area about 0.25 cm. in diameter. There was no herniation at this level, however, and exploration of the intervertebral canal on the left at this level revealed no herniation. A block containing the eroded annulus was cut out and the degenerated nucleus thoroughly curetted away. The intraspinal aspect of the disks at the fourth and fifth lumbar spaces was normal, and the annulus at both places was of normal firmness. However, after complete exposure of the intervertebral canal at the fourth lumbar disk on the left, it was noted that the intracanalicular portion of the fourth lumbar nerve was displaced dorsalward. It was not until this portion of the nerve was reflected dorsalward and mesialward that a large piece of sequestered nucleus was uncovered. It fairly popped out of a pocket which had ruptured within the confines of the intervertebral canal, and the remainder of the disk was of normal integrity. The severe compression of the fourth lumbar root in its canal on the left accounted for the hypalgesia in the fourth lumbar distribution and for the diminished knee jerk without diminution of the ankle jerk. The patient was completely relieved of the sciatic pain on awakening from the anesthesia.

## XI. POSTOPERATIVE CARE

Throughout this thesis it has been difficult to separate sharply the degenerating from the herniating disk in respect to surgical considerations. Since the herniating, or ruptured, disk is only an advanced stage of the degenerating disk, the problems involving operation and postoperative care are essentially the same. Treatment involves three essential objectives: (1) relief of compression of the root if it exists, (2) stabilization of the lumbar or lumbosacral joints and (3) release and relaxation of spastic muscles about the lumbosacral region and restoration of strained ligaments.

Relief of compression of a root is simple enough and is the easiest part of the contract.

Stabilization of the lumbosacral portion of the spine is contingent on the development of a firm fibrocartilaginous scar which fixes the adjacent vertebral bodies (see section on pathology).

Relaxation of spastic muscles and restoration of strained ligaments and tendons may require persistence and patience. Toward this end the maintenance of the lordotic posture is important. Boards are placed crosswise under the mattress so as to lift the patient in a manner that will support the small of the back, and the patient is encouraged to sleep on his back for the most part. This is a simple but, I feel, an essential part of the treatment. Almost every patient whom I have treated has agreed, without reservation, that this arrangement has been greatly beneficial to him, and those who have attempted to discard it have readopted it of their own volition. Many patients even before operation have discovered for themselves that sleeping on the floor is preferable to sleeping on a mattress. A patient with a weak back should divorce himself forever from the soft, downy mattress on which a partially flexed posture is assumed. The extended posture with emphasis of lordosis of the lumbar region releases tension on the ligaments, muscles and tendons of the lumbosacral portion of the spine and breaks the cycle of spasticity, deformity and irritability. Just because herniation of a disk has been treated surgically and the compression of the roots relieved, the tangible objective, it does not follow that these long-standing reactionary factors will immediately abate. This third phase of the treatment is paramount in the obtaining of optimum results. In cases in which chronic pain low in the back is a part of the syndrome, the patient should have check-up examinations at intervals of about one month after the operation until maximum improvement has been attained. He should be cautioned continually to adhere to the prescription, because it seems normal for the average patient to "forget" or to "misunderstand" the directions. Neither the doctor nor the patient need be disheartened if recovery is delayed for periods as long as eight months to a year. The patient should be reassured and the purposes and objectives of the

treatment explained in terms that he can grasp, because in any long-continued treatment that seems slow in attaining success it is only natural for the patient to lose faith. It is part of the treatment to proffer periodic reassurance and rechecking in order to keep the patient from deviating from the prescription. These remarks concerning postoperative care relate, of course, to cases of advanced and severe herniating disks. Many patients, especially those who have simple and limited herniated disks, never feel that it is necessary to have the first check-up examination. There is obviously a complete gamut of variations in respect to the extent of the pathologic changes and to the element of time in response to treatment. If optimum results in the management of the pathologic disk are to be uniformly attained, then it is certain that the patient who has had a ruptured disk cannot always be sent on his way as cured because the wound is healed and he is free of fever.

The manner in which the mattress is adjusted merits emphasis, because the wrong adjustment may be harmful. Boards 1 inch (2.5 cm.) by 6 to 10 inches (15 to 25 cm.) are suitable. Leaves from the dining table are often convenient. The mattress should preferably have no inner spring. The board should be placed directly under the mattress and crosswise, so that the ends rest on the sideboards of the bed. Sometimes two or three boards on top of one another are necessary, depending on the mattress, to obtain the proper-sized hillock or smooth ridge across the mattress. This ridge should be only wide enough to accommodate the curvature of the lumbar region and high enough to lift the lumbar portion of the spine a little and maintain lordosis of the lumbar region that is moderately exaggerated for the individual patient. There should be no sharp ridges that are uncomfortable. The ridge should not be located under the hips or under the chest or costal margins. This not only defeats the purpose intended but provokes other postural pains in the back and hips.

Some patients have been discharged from the hospital completely free of their former pain of herniating disk only to call after two or three weeks and complain of what they think is a return of the old trouble. A visit to the home reveals that instructions have not been carried out, and examination reveals what I refer to as a "spastic back," without the description or findings of pain from compression of a root. The patient maintains a somewhat flexed posture and is reluctant to extend his back. The erector spinae muscles are spastic, and there is usually tenderness parasacrally. It is the picture of tendinomuscular pull or strain. Appropriate muscles of the back become spastic in an attempt to splint the lumbar and lumbosacral segments. Rest in bed for a few days or a week on a properly fixed mattress, providing a hillock under the small of the back and occasionally a 10 pound (4.5 Kg.) traction to each leg, has given complete relief. Heat is a



valuable adjunct. Such a postoperative complication is in such a case again due to an insufficiently stable joint. After thorough curettement of a disk, I feel that the patient should remain in bed for an absolute minimum of two weeks, and it should be remembered that dependable fusion and firm intervertebral fixation probably require about two to three months. Casts or other external fixation or tibial bone grafts are rarely necessary. The scar will form, and fixation will obtain though the patient is ambulatory, and when the policies given here have been observed the results have been good.

Some patients who have severe herniating disks will continue to complain of some residual sciatic pain after operation. This is not surprising when one witnesses the swollen inflammatory state of the compressed nerve root, but if the operation has been thorough this residual sciatic pain will disappear with time. Subjective numbness in the distribution of a nerve root may last indefinitely and is due to loss of fibers of the sensory root. The patient should be apprised of the difference between numbness and pain.

A certain amount of stiffness of the lumbosacral portion of the spine is a natural consequence of the operation and is the objective that is bargained for. An intervertebral disk that is a fibrocartilaginous scar is certainly not so mobile as a normal disk, but relief of the patient's discomfort is contingent on stabilization and immobilization of the joint.

Pain low in the back and sciatic pain incident to pathologic changes in the intervertebral disks can now be adequately and satisfactorily treated, with good results, but the situation is not foolproof. Patience and understanding of all the factors involved are paramount to the best results.

If the operation is thorough and the wound is given a chance to heal well and escapes infection, braces and belts are not to be encouraged except in rare instances. Strange as it may seem, the back is not weakened by the operation described but strengthened considerably more than it was previous to operation. The relief of chronic pain low in the back and the episodes of acute pain bear out this statement.

## XII. RESULTS

*Industrial Implications.*—When the surgical treatment of degenerating and herniating disks is carried out as outlined, the results on the whole are highly satisfactory. However, when speaking in terms of results, one should have clearly in mind the type and degree of pathologic changes in the disks that exist in the individual case. Broadly speaking, one can visualize the degree or extensiveness of disintegration as ranging from small pocketed sequestration, on the one hand, to disintegration of the entire disk, on the other. In the first case, the symptoms and signs may be only those of compression of a root and its attending sciatic radia-

tion. There is usually no complaint of chronic pain low in the back. When the compression of the nerve root is relieved by elimination of the small herniation in these cases, this being done either by minimal or by maximal exposure, the results are not infrequently 100 per cent. These are relatively simple cases. The indications are clear, the surgical problem is not difficult and relief is usually immediate. The situation is not complicated by an unstable intervertebral joint. On the other hand, when one is dealing with advanced degeneration of the disk as a whole, with or without herniation, the problem is considerably more involved. The patient should remain in bed longer after operation and should avoid heavy labor for a longer period. Such patients will usually complain of chronic pain low in the back which has existed for years, augmented from time to time by acute "toothache-like" pain deep in the gluteal region. One might alleviate compression of a root and true sciatic radiation, if it exists, in short order, but one cannot reasonably expect to abolish the factor of pain low in the back without time, patience and an understanding of the objective to be gained. The development of a good scar that adequately fixes adjacent vertebrae requires at least two to three months and even longer in many cases. During this time, the extended posture of the lumbar portion of the spine should be maintained while the patient is in bed and out and strain on the back should be avoided. Patients in these cases almost uniformly feel great relief while in bed and at the time they are discharged from the hospital. The greater percentage continue to do well, and strong backs develop. Some are not so careful and fail to observe the rules. They may experience further episodes of acute pain. They yield to treatment, however, and in time, as the lumbosacral joint grows stronger, the acute episodes cease to occur and the residual pain low in the back fades away. In 5 cases of severe herniated disks I have prescribed a steel stay corset as an aid in partially immobilizing the lumbosacral portion of the spine and maintaining correct posture. I feel that this is an advantage for a few patients who, for economic reasons, would like to return to work at an early date, if the type of work would not be too encumbered by the corset.

It is true that if a patient with an acute pain low in the back of the type under discussion is put to bed with extension of the lumbar region and with or without traction for a week, he, too, will usually feel relieved without operation. The basic cause has not been remedied, however, and he is subject to the same repeated cycles of pain. The objective of operation is to establish a satisfactory permanent stabilization.

These remarks are intended as explanation and not apology for the fact that results in such cases may at first seem poor. It is a rare patient who does not bear good affidavit for his treatment after six months. Also, as might be expected when such severe lesions are being dealt with, few patients can be classed as 100 per cent relieved. The greater

percentage will be 60 to 90 per cent relieved. I have had patients say with profound gratitude that they are able to get a comfortable night's rest for the first time in years or are able to sit for long periods or stoop and otherwise put their backs to test without paying heavily the price of gnawing and aching pain low in the back.

Considerable criticism is yet extended by some in respect to the merits of operation on even the profound herniating disk. I feel that physicians—not the patient—have perhaps expected too much in terms of results. It is strange that it is so, because previous to 1934 a patient with herniating disk and incapacitating and agonizing sciatica went without the specific treatment that he can be given now. He was a victim of "shots in the hip," stretching of the sciatic nerve, injections of procaine hydrochloride, isotonic solution of sodium chloride and alcohol into the sciatic nerve, repeated epidural or parasacral injections of procaine hydrochloride or periods of hospitalization for bed rest, traction and similar treatment, all of which were obviously of little avail as a cure. A patient with proper surgical treatment of a herniating disk now bears the only testimony that is needed. Assuming that he were only 50 per cent relieved, I—and I know the patient—should consider the relief a real achievement.

The degenerating-herniating disk is a serious lesion and should be deserving of the same consideration as that given to the dislocation of a major joint or fracture of a long bone. One could hardly expect, after the most expert surgical treatment, to reduce uniformly the disability of a patient to zero or that an enlisted man could withstand the rigors of modern military training. With this, as with any other major surgical problem, the relief of illness and pain is the first objective. Physical and industrial rehabilitation is the second.

The herniating disk has become of considerable medicolegal and industrial import. Matters relating to the etiology and to the so-called specific accident which is thought to be responsible for the injury to the disk cloud the issue in respect to liability and compensation. Often the correct diagnosis is not made until the time limit (according to the statute of limitations) from the "specific accident" has passed. This relieves the insurance company of liability and places the patient at a disadvantage. In the state of Colorado, if I am correct, these problems have been obviated to some extent for the present by a ruling that even though a pathologic disk may have preexisted an acute attack of pain while in the line of duty constitutes an aggravation of the condition and renders the insuring company liable. In view of the specialized nature of the syndrome and the reasonable likelihood that the correct diagnosis may be long overlooked through no fault of the patient, the problem of reopening the case after the time limit has expired becomes a pertinent one.

In my experience with industrial cases I have felt that the patient's disability has ultimately been reduced from almost total disability to 5 or 10 per cent in most of the cases. Some stiffness of the lumbosacral portion of the spine usually persists, and it is a result that is intended. It is usually of such a degree as to constitute, in my opinion, a 5 per cent disability for at least a year.

### XIII. SUMMARY AND CONCLUSIONS

Evidence has been presented to substantiate the proposition that degeneration and disintegration of the intervertebral disk in the low lumbar region is the predominant cause of chronic pain low in the back. Herniation and rupture of a disk is an advanced stage of degeneration and is associated with the syndrome of compression of a nerve root. The process of degeneration of the nucleus pulposus and annulus fibrosus described is a necessary prerequisite to herniation and may prove to be, for the most part, of developmental origin. Whatever role trauma may play, it is only an accessory one.

The syndrome of chronic pain low in the back is due to a weakened lumbar or lumbosacral joint. The syndrome of radiating pain in sciatic distribution is due to compression of a nerve root. These two syndromes are separate and distinct entities. They are due to different aspects of the same pathologic process and hence may exist independently or combined.

Treatment of the degenerating disk consists in removal of the pathologic tissue. The result is contingent on the development of a new fibrocartilaginous disk that serves to fuse the adjacent vertebrae into a mechanical unit.

There are a number of different types of herniation which have been classified and given separate consideration. Special emphasis is placed on herniation within an intervertebral canal—a disclosure that broadens the variety of pathologic changes in disks and widens the scope of operations.

632 Republic Building.

# ACUTE SUPERIOR MESENTERIC ARTERY THROMBOSIS

Recovery Following Extensive Resection of Small and Large Intestines

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NEW YORK

WHILE I was on duty at an evacuation hospital functioning in February 1945, amid the rush of caring for battle casualties it was interesting to be confronted with an unusual acute condition within the abdomen which required operation.

An infantry private first class, 19 years old, was admitted to the hospital on February 16, with shell fragment wounds of the left arm and right thigh. Shortly after admission these wounds were excised, with the patient under anesthesia induced by pentothal sodium. A foreign body was removed from the wound in the right thigh. The patient made an uneventful recovery and was out of bed on the third day. He was scheduled to be evacuated to an Army convalescent hospital on the fourth day after operation.

On the evening of the third day, shortly after eating his evening meal, the patient was seized with severe pain in the upper abdominal region. He vomited, and diarrhea developed. The vomiting continued all evening. The temperature and pulse were normal. The blood count, taken around midnight, revealed a white blood cell count of 17,000, stab forms 10 per cent, polymorphonuclear leukocytes 81 per cent, lymphocytes 6 per cent and monocytes 3 per cent. Physical examination revealed a soft but tender abdomen. There was no localized point of tenderness. The severity of the pain was out of all proportion to the physical signs. After observation by the surgical team on duty in the ward, morphine hydrochloride,  $\frac{1}{4}$  grain (0.01 Gm.) was given hypodermically. There was no relief of pain. Early the next morning I was called to see the patient. The temperature and pulse were still normal, but on physical examination there was some bilateral rectospasm and tenderness in the midabdomen. There was no tenderness over McBurney's point. Both of the inguinal grooves were soft and not tender. The blood cell count was now white blood cells 22,300, stab forms 17 per cent, polymorphonuclear leukocytes 72 per cent lymphocytes 8 per cent and monocytes 3 per cent. Results of examination of the chest were normal. The urine was normal except for rare red blood cells, occasional casts and sulfa-like crystals. The patient had been receiving the routinely given sulfadiazine.

The case was considered one of an acute condition within the abdomen, with a differential diagnosis of possible perforating gastric ulcer, acute cholecystitis, volvulus or mesenteric artery thrombosis. It was not considered to be acute appendicitis. The vomiting had persisted.

A roentgenogram of the abdomen with the patient in the erect posture was ordered. This showed no evidence of free gas under the diaphragm. The

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temperature had risen to 100.2 F. The pulse rate was 120, and the respiratory rate was 36. Exploratory laparotomy was indicated.

*Operation.*—The operation was started with the patient under spinal anesthesia induced by 150 mg. of procaine hydrochloride. Because of the findings, the anesthetic was changed to general open ether with endotracheal tube.

*Findings.*—A right rectus incision was made. The peritoneal cavity contained a moderate amount of clear fluid. The presenting small intestines were dark blue-black but were not distended. There was a pronounced gangrenous odor. The incision was lengthened upward and downward. There was no evidence of volvulus. The approximate upper 20 inches (51 cm.) of the jejunum was viable, and pulsation of the arteries could be seen as they passed from the mesentery into the jejunum. At a point about 20 inches from the fossa of Treitz, the pulsation of the arteries suddenly ceased and the color of the intestine changed just as abruptly. Following the mesentery down toward the right iliac fossa, all the arteries were pulseless. The mesentery was without fat, and all the vessels could be seen readily. Passing down the jejunum and ileum, one quickly observed that all the small intestines were blue-black. Surprisingly, the appendix, cecum, ascending colon, hepatic flexure and beginning of the transverse colon were also found to be blue-black. The ileocolic and right colic arteries with their branches were pulseless, but near the midtransverse colon the color of the colon became pink and good pulsation was visible. Here again there was a sharp line of demarcation between the viable and the necrotizing colon. The midcolic artery was found to be pulsating well. With these findings, a diagnosis of thrombosis of the superior mesenteric artery just below the origin of the midcolic artery was made. The mesentery was filled with greatly enlarged, soft lymph nodes.

*Procedure.*—It was realized that only about 18 inches (46 cm.) of the upper jejunum would remain after resection of necrotic small intestine and also that all the large intestine up to the midtransverse colon would have to be resected. However, there was no choice, and radical excision was indicated. Naturally, I feared that not enough bowel surface would remain for digestion and absorption. It was realized that inanition might ensue. Technically the resection was simple. On division of the mesentery near its root, the thrombi could be seen within the lumen of the vessels. The jejunum was divided and both ends closed; the proximal end was inverted. The transverse colon was divided and both ends closed and the distal end inverted. The entire necrotic bowel was removed in one mass. An isoperistaltic, side to side jejunocolostomy was performed. The aperture was about 1½ inches (4 cm.) long. The suture line was reenforced by the placing of the omentum over it. The denuded surface in the right inguinal groove was peritonealized. Five grams of sulfanilamide powder was introduced into the right side of the peritoneal cavity, which indeed seemed empty. The abdomen was closed with through and through silk sutures, and the rectus sheath was closed with interrupted chromic surgical gut sutures. The skin was closed with interrupted silk sutures.

*Specimen.*—Unfortunately, with the volume of battle casualties (eight operating tables were functioning at the time), the specimen, because of its bad, gangrenous odor, was put into the potbelly stove and burned by the operating room sergeant. Therefore, the opportunity of carefully examining it and removing a node for pathologic examination was unfortunately lost.

*Postoperative Course.*—A Levine tube was passed into the stomach, and Wangensteen suction was applied. Penicillin and sulfadiazine were given for

the first three days. The patient stood the operative procedure well. Medicaments, 5 per cent dextrose in isotonic solution of sodium chloride and 10 per cent dextrose in distilled water in the ratio of 2:1, were administered intravenously. Thiamine hydrochloride was also given. Two transfusions of 250 cc. of whole blood were given. After each transfusion the patient had a fever reaction. Therefore they were discontinued. As soon as it was ascertained that the anastomosis was functioning well, the Levine tube was removed and feedings were started. Just as soon as some solid food and fluids were given, the patient complained immediately that his bowels had to move. The fluid seemed to run right through the remaining intestines. The patient therefore insisted on remaining on the bedpan for long periods. He was afraid to get off of the bedpan. A colonic tube was then left in the rectum and drained into a container on the ground.

It was felt that the patient might benefit by the intravenous use of casein hydrolysate and thiamine hydrochloride (vitamin B<sub>1</sub>), 10 mg.; riboflavin (vitamin B<sub>2</sub>), 5 mg.; nicotinic acid, 20 mg.; and ascorbic acid (vitamin C), 100 mg. daily. Only thiamine hydrochloride and ascorbic acid were available and therefore employed.

During the convalescence at our hospital the patient coughed and expectorated a great deal of thick phlegm. Physical examination, corroborated by roentgenologic examinations, revealed some evidence of atelectasis or infarct of the right lower lobe of the lungs. With encouragement of coughing, deep breathing into a paper bag and frequent change of posture, this condition improved.

Five days after the operation the hematocrit level was 32.8 per cent, the hemoglobin content 11 Gm., and the total protein content 6.5 Gm. per hundred cubic centimeters. The protein intake was kept up by the use of plasma intravenously. The fluid balance was also carefully maintained.

*History.*—When the patient had improved sufficiently, a careful history was obtained because of the interesting and unusual findings.

*Family History:* There were four siblings. The mother and father were healthy and well. There had been no operations and no serious illnesses.

*Habits:* The patient smoked one package of cigars a day and used no alcohol or drugs. He was married just before he entered service. He denied having venereal disease. He had had the usual childhood diseases. By occupation, he was a truck driver and defense worker and worked with molten metal.

*Systems:* Neurologic examination showed that occasionally he felt light headed. There was no history of fainting, convulsions or paresthesias, but he had had occasional headaches. The circulatory system was normal. Gastrointestinal examination (see present illness) showed that between attacks his appetite was good. The urinary examination was noncontributory.

*Present Illness:* Since the age of 10 to 11, the patient had been having attacks of cramplike pain in the abdomen, which had occurred several times a week to every few months. They had never been sufficiently severe for the patient to see a doctor. The intensity varied from mild to severe. They lasted from an hour to several days. During the attacks the patient vomited and had anorexia. The present illness started the day the patient was wounded. He had had mild cramps for two days before he was wounded but did not say anything about it. They became severe the third day after he was wounded, at the time when he was to be discharged from the hospital.

*Physical Examination.*—The physical examination gave negative results, as it had on admission, except for the acute condition within the abdomen, as described.

There was a soft blowing systolic murmur over the area of the pulmonary artery. Otherwise the heart was normal.

The patient was evacuated by air to the United Kingdom on the tenth day after the operation.

*Follow-Up Report.*—I had requested that the patient drop me a line as to his further progress during evacuation. I received a letter from the patient written a few days after he had arrived at a general hospital in the Zone of Communications. I then wrote to the chief of the surgical service of this hospital and received the following most interesting report from Lt. Col. Fred H. Miller. The patient had been admitted to this general hospital the day after he left the evacuation hospital. I quote herewith: "The patient was admitted to the General Hospital on March 3, 1945. His general condition appeared good. He was having six to seven liquid stools daily, with mild crampy abdominal pain. The wound was healing well. The patient was placed on a bland, low residue, high caloric diet. He was given bismuth subcarbonate, 30 grains (1.9 Gm.); tincture of opium, 10 minims (0.6 cc.) three times a day, one-half hour before meals; riboflavin, 10 mg. daily by mouth; thiamine hydrochloride, 10 mg.; nicotinic acid, 25 mg., and ascorbic acid, 200 mg. intravenously daily. On March 4, 1945 the bowel movements decreased to four liquid stools. At 10 p. m. the patient suddenly experienced a sharp pain just below the right knee in the calf, which progressed and radiated down to the toes. The foot was blanched, and no pulsation could be felt in the dorsalis pedis, posterior tibial or popliteal arteries on that side. Pulsation was also absent in the left dorsalis pedis and posterior tibial arteries, but the temperature and color of the left foot were normal. The patient was given  $\frac{1}{4}$  grain (0.01 Gm.) of morphine immediately, with little relief. He was then given  $\frac{1}{2}$  grain (0.03 Gm.) of papaverine intravenously, and shortly thereafter the pain subsided completely but pulsation was still absent in both feet, and the right foot continued to show impairment in circulation.

On March 5, 1945 at 2 a. m. the patient was taken to the operating room, and a paravertebral block on the right side was done with 10 cc. of 1 per cent procaine hydrochloride. This caused some improvement in the peripheral circulation, manifested by warmth and dryness but no pulsation. Thereupon with the patient under anesthesia induced by 120 cc. of 0.5 per cent procaine hydrochloride solution by local infiltration, a 6 inch (15 cm.) incision was made over the right popliteal artery. Gastrocnemius bellies separated in the midline. The artery was exposed and showed no pulsation below the area of the knee joint. The artery was incised for a distance of 0.5 cm. There was no bleeding from the lower end but free bleeding from the upper end. Suction was applied, and about  $1\frac{1}{2}$  inches (4 cm.) of organized clot was removed. There was free bleeding from the lower end after this. Heparin, 5,000 units, was instilled in the artery, and the vessel was closed with three interrupted mattress sutures of 0000 silk. Closure was done with interrupted sutures in three layers. The artery pulsated below the suture on closure. The right foot was not blanched, and faint pulsation of the posterior tibial and dorsalis pedis artery could be felt at the end of the operation. The patient stood the procedure well. The patient returned from the operating room in good condition, with continuous intravenous administration of heparin. The color of the right foot remained good, and about six hours after the operation pulsation could be felt in the right posterior tibial artery but not in the left posterior tibial artery. The administration of heparin was continued, and papaverine, 1 grain (0.06 Gm.), was given every four hours.

On March 6, 1945 the general condition had remained good, the patient having about four large liquid bowel movements daily. Pulsation in the dorsalis pedis and posterior tibial arteries in both feet could be felt. The administration of



heparin was continued but the administration of papaverine was discontinued. The hemoglobin content was 82.5 per cent, hematocrit reading 38.6 per cent and protein level 6 Gm.

On March 7, the general condition of the patient was good. Bowel movement was the same. The circulation in both feet was excellent. The diet was changed to five feedings daily. Administration of bismuth was discontinued. One unit of blood plasma was given.

From March 7 to March 14 the condition of the patient continued to improve. The wounds were healing well. He continued to have about four large liquid bowel movements daily, putting out about 2,500 cc. of fluid by this route. His daily urinary output was about 500 to 600 cc. at first, but later this rose to 1,500 cc. per day. He showed no decrease in hemoglobin, chlorides or blood protein content.

With the wounds well healed, the general condition of the patient good and the circulation of the extremities good, it was decided that he could be safely evacuated to the Zone of the Interior by air as a litter patient; this was accomplished on March 26. On April 12 I received a letter from the patient, in which he stated that he was going on a three day pass and was going home for the weekend and then he was going to get a thirty day furlough. His return address was given as one of the named general hospitals in the states."

I then wrote to the chief of the surgical service of this hospital in the Zone of the Interior. I received the following reports from Lt. Col. John H. Gibbon Jr. The first report from Colonel Gibbon was dated June 5. I quote: "The patient arrived at this hospital in excellent condition, weighing 105 pounds (47.6 Kg.), on April 8. He has just returned from a thirty day furlough. While at home he avoided roughage and fatty and greasy foods but otherwise ate a normal diet. His bowels move two to three times daily. The stools are soft and frequently formed. He now weighs 113 pounds (51.3 Kg.); his best weight had been 140 pounds (63.5 Kg.), and he weighed 138 pounds (62.6 Kg.) when he was wounded. He shows no evidence of any vitamin deficiency. He looks normally nourished and appears strong and healthy. There is no circulatory deficiency in his right foot, and both pulses are palpable. Blood studies are normal except that he has slight haemoconcentration. On April 27 his hematocrit reading was 48.5 per cent. On April 13 there were 4,900,000 red blood cells and 4,000 white blood cells. The hemoglobin content was 15.9 Gm. (rechecked), the nonprotein nitrogen level 37 mg. and the sugar content 102 mg. per hundred cubic centimeters and the chloride level 99 milliequivalents per liter. His scar is firm, and there is no incisional hernia."

In further follow-up I wrote Colonel Gibbon once more and received the following report from him, written on August 13. "There is little additional information to give you concerning your patient. He received his discharge from the Army last week, after completion of some gastrointestinal studies. His motility test with carmine was forty-eight hours, which was considered normal. His weight was 115 pounds (52 Kg.). He has two soft stools daily that are mushy, but he has had no diarrhea. His blood count on June 26 showed 5,000,000 red cells, 6,200 white cells and 15.5 Gm. of hemoglobin per hundred cubic centimeters. He was tested for a number of days on several different diets. On all these diets there were large amounts of fat and starch in his stools. This was particularly pronounced on the high fat diet. It was also true on a medium carbohydrate and low fat diet. On a high protein, medium carbohydrate and low fat diet he lost weight. The diet on which he did best was a high carbohydrate, low fat and medium protein diet. All glucose tolerance tests were normal. Blood cholesterol, phosphorous, lipid and amylase levels were all within normal limits. Blood

chloride levels were also normal. The total serum protein content was 5.8 Gm. per hundred cubic centimeters, albumin 3.6 Gm. and globulin 2.2 Gm. The general condition of the patient was excellent, and I am sure that he will get along all right at home."

A letter received from the patient at the end of November 1945, from his home in the Middle West, states that he is well. His weight is now 120 pounds (54.4 kg.), and he has two to three bowel movements a day.

#### SUMMARY

A report is made of a case of an acute condition of the abdomen, requiring surgical intervention, complicating a battle-incurred wound by a shell fragment in the left arm and right thigh.

At operation it was found that the patient had a thrombosis of the superior mesenteric artery at a point just distal to the origin of the midcolic artery. This caused necrosis of all but the upper approximate 18 inches of the jejunum and all the large bowel up to the midtransverse colon. Resection of the necrotic bowel and a jejunocolostomy were performed.

The patient made a good surgical recovery and was evacuated by air on the eleventh postoperative day to a general hospital in the Zone of Communications.

At this hospital further arterial thrombosis developed, this time of the popliteal artery. An embolectomy on the right popliteal artery was successfully performed. Heparinization was employed here. It had not been available at the time of our intestinal resection at the forward echelon. The patient made a good recovery.

The patient was evacuated by air from the Zone of Communications to a named general hospital in the Zone of the Interior. Here he was studied, and it was found that he was absorbing sufficient nourishment from the remaining intestines to maintain good health.

The patient was discharged from the army and returned home. He was doing well nine months after the operation.

#### CONCLUSIONS

Removal of the entire small intestine except about 18 inches of the upper jejunum and removal of the large bowel to the midtransverse portion is apparently possible without serious digestive disturbances and inanition.

The patient did best on a high carbohydrate, low fat and medium protein diet.

Major Martin, of the named general hospital, will later report further nutritional studies of this case.

The etiology of the multiple major arterial thromboses in an apparently healthy young soldier of 19 years presents a fascinating problem.

Lieutenant Colonel Miller and Lieutenant Colonel Gibbon kept me informed of the progress and follow-up of the patient in this somewhat unusual case.

## ZEPHIRAN CHLORIDE FOR THE PREOPERATIVE PREPARATION OF THE HANDS

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**Z**EPHIRAN chloride, a mixture of high molecular alkyl-dimethyl-benzyl ammonium chlorides, is a cationic detergent and germicide. Domagk,<sup>1</sup> Dunn,<sup>2</sup> Baker and colleagues,<sup>3</sup> White and colleagues,<sup>4</sup> Walter,<sup>5</sup> Schumacker and Bethea,<sup>6</sup> Hauser and Cutter<sup>7</sup> and others have appraised its value as a germicide and pointed out its usefulness in the field of surgery.<sup>8</sup> It is the purpose of this report to present the results obtained while its value was being investigated in use as a mechanical and chemical cleansing agent for the preoperative preparation of the hands, to compare its worth as a detergent when used for this purpose with that of medicinal soft soap and to compare its merits as a bactericide with those of 70 per cent alcohol when employed as a chemical cleansing agent.

Domagk<sup>1</sup> first pointed out some of the physical properties of zephiran chloride. It is a colorless, almost odorless liquid, which foams on shaking and is slightly alkaline to litmus. It does not precipitate with alkalis and remains clear when tap water is added, and there is

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From the Department of Surgery, Duke University School of Medicine and Duke Hospital.

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no precipitate or loss of bactericidal power with the addition of acids. It is compatible with most substances with which it is likely to come in contact in the operating room.<sup>7</sup> It is stable over a wide range of temperatures; freezing, storage at above 50 C. for eighteen days and storage at room temperature for over eight months caused no apparent loss in germicidal efficacy.<sup>2a,b</sup> It has a detergent and emollient action and is not irritating to the skin. The hands when wet with zephiran chloride solution become soft and smooth and remain so for several hours after the skin has become dry. Soap exerts an inactivating influence on zephiran chloride.

Miller and his associates<sup>9</sup> have demonstrated that zephiran chloride deposits an invisible film on the hands. The film retains bacteria beneath it and is said to be extremely resistant to ordinary mechanical trauma. This may in part be responsible for the decrease in the number of bacteria that can be removed from the cutaneous surface after zephiran chloride is used. Zephiran chloride also kills bacteria, and Valko and Dubois<sup>10</sup> have shown that the "killing" action of the surface-active cations on bacteria can be reversed under certain conditions by detoxication with a high molecular anion. They stated that the initial process in the action of surface-active cations can be satisfactorily described as a reversible adsorption by the bacteria, which function as cationic exchangers. Little is known about the course of events which follows this primary process and finally leads to the death of the bacteria.

#### PLAN OF EXPERIMENTAL STUDIES

Since zephiran chloride is a detergent and also a germicide, it can be employed for both mechanical and chemical cleansing of the skin. While these investigations were being carried out, it was desirable (1) to establish its value as a detergent for scrubbing the hands and arms and to compare its worth when used for this purpose with that of medicinal soft soap and (2) to determine its value in use as a chemical cleansing agent and to compare its worth with that of 70 per cent alcohol. It was also desirable to establish the necessity for mechanical cleansing of the hands and arms between clean operations when zephiran chloride is employed as a chemical cleansing agent. Because of the fact that soap exerts an inactivating influence on zephiran chloride, it was advisable to determine whether an aqueous solution of zephiran chloride can be used in the operating room as a chemical cleansing agent after one has scrubbed with soap and water.

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10. Valko, E. I., and Dubois, A. S.: The Antibacterial Action of Surface Active Cations, *J. Bact.* **47**:15-25, 1944.

## GENERAL PROCEDURE

Mechanical cleansing of the hands and arms was performed by scrubbing for eight minutes, a 1:500 aqueous solution of zephiran chloride and medicinal soft soap being used for comparison as detergents. Two brushes were used, one being discarded after the hands were scrubbed for three minutes. The nails were cleaned with an orangewood stick after the first brush was discarded. Tap water was used in combination with the detergents in all these experiments. After mechanical cleansing was performed, the hands and arms were washed with a washcloth for three minutes in a basin containing  $\frac{1}{2}$  gallon (1.9 liters) of the solution used for chemical cleansing. Immediately after preparation of the hands, a culture was taken of the solution after the hands up to the wrists had been washed for one minute in a basin containing 500 cc. of sterile isotonic solution of sodium chloride. Five cubic centimeters of the isotonic solution of sodium chloride was removed from the basin with a sterile pipet and placed in a blood-dextrose agar pour plate and incubated for forty-eight hours. The colonies on the plate after forty-eight hours of incubation were counted, and the number of bacteria in the 500 cc. of isotonic solution of sodium chloride was estimated.

After the first culture was taken, sterile gloves were put on the hands, the dry technic being used. A rubber band was placed around the arms at the tops of the gloves to prevent, so far as possible, contaminated perspiration from getting into the gloves. Gowns were not worn. After a period of one hour had elapsed, the gloves were removed and another culture was taken as previously described. During this one hour period the subjects who assisted in these experiments continued their usual hospital duties, and no attempt was made to keep the outsides of the gloves sterile.

After the second culture was taken the hands were washed with a washcloth for three minutes in the solution used for chemical cleansing, and a third culture was taken in the manner as described in the first paragraph. Chemical cleansing was performed after gloves had been worn for one hour in an effort to determine the necessity for mechanical cleansing between clean operations.

When cultures were taken by this method, a small amount of the chemical cleansing agent was washed from the hands into the isotonic solution of sodium chloride and subsequently transferred to the culture plate. Although these substances were diluted considerably, it was necessary to determine whether their presence in the culture mediums would cause sufficient bacteriostasis to alter the results. Five experiments were performed in which the gloved hands were immersed in a 1:1,000 aqueous solution of zephiran chloride and in a 70 per cent solution of alcohol. These substances were washed off the hands into 500 cc. of sterile isotonic solution of sodium chloride. Five cubic centimeters of the isotonic solution of sodium chloride was placed in tubes containing 10 cc. of dextrose agar and 2 cc. of blood which had been previously inoculated with 0.1 cc. of an emulsion of *Staphylococcus aureus* bacteria. There was no significant difference in the number of colonies of bacteria growing on the plates after forty-eight hours' incubation when compared with cultures that were inoculated as controls. The alcohol and zephiran chloride washed from the hands were diluted by the isotonic solution of sodium chloride and blood agar to such an extent that bacteriostasis sufficient to alter the results did not occur.

Many factors influence the number of bacteria remaining on the surface of the hands after mechanical and chemical cleansing. It was thought, however, that by the performance of the same experiment fifteen times the results would be satisfactory for comparison. It is not felt that the absence of growth of

organisms in cultures taken in this manner indicates that the hands are sterile. It appears that absolute sterility of the skin of the hands and forearms is impossible to attain.<sup>11</sup>

These experiments were performed by subjects in groups of five. Subjects were members of the resident house staff, nurses assigned to the operating room and medical students who were familiar with the art of scrubbing. The hands were not washed and the nails were not cleaned before the experiments were begun. No subject performed the experiment oftener than once each day. The temperature could not be kept constant. Every precaution was taken to prevent the isotonic solution of sodium chloride in the basins from becoming contaminated with air-borne bacteria. The basins were covered with sterile towels, and the experiments were performed in the operating room under bactericidal irradiation to further minimize contamination from the air.

TABLE 1.—*Bactericidal Effect of Soap and Water Plus Alcohol*

Results of Cultures after Scrubbing for Eight Minutes and Washing in 70 per Cent Alcohol for Three Minutes.

|         | Culture After<br>Preparation of the<br>Hands,<br>Number of Bacteria | After Gloves<br>Were Worn for<br>1 Hour,<br>Number of Bacteria | After Washing in<br>70 per Cent Alcohol<br>3 Minutes,<br>Number of Bacteria |
|---------|---|--|---|
| 1.....  | 2,500   | 800  | 2,700   |
| 2.....  | 1,900   | 2,200  | 200   |
| 3.....  | 14,400  | 43,200   | 4,800   |
| 4.....  | 208,000   | 171,600  | 25,600  |
| 5.....  | 4,800   | 24,200   | 1,600   |
| 6.....  | 9,000   | 20,000   | 6,600   |
| 7.....  | 500   | 800  | 6,900   |
| 8.....  | 83,200  | 49,600   | 64,000  |
| 9.....  | 1,900   | 9,100  | 2,700   |
| 10..... | 1,600   | 8,800  | 2,200   |
| 11..... | 3,200   | 2,500  | 9,200   |
| 12..... | 300   | 100  | 800   |
| 13..... | 900   | 100  | 700   |
| 14..... | 1,100   | 1,900  | Negative  |
| 15..... | 100   | Negative   | 400   |

#### EXPERIMENTS AND RESULTS

In the first experiment the hands and arms were prepared by scrubbing for eight minutes with medicinal soft soap and tap water and by washing for three minutes in 70 per cent alcohol. The results are listed in table 1. All cultures taken immediately after preparation of the hands were positive for bacterial growth. Only two negative cultures were obtained in the entire series. In eight instances there was an increase in the number of bacteria removed from the surface of the hands after gloves had been worn for one hour. Only one culture, taken after chemical cleansing had been performed for the second time, was negative for bacterial growth.

To establish the value of zephiran chloride as a chemical cleansing agent for the hands and arms, the following experiments were performed. The hands and arms were prepared by scrubbing with

11. Lovell, D. L.: Skin Bacteria: Their Location with Reference to Skin Sterilization, Surg., Gynec. & Obst. 80:174-177, 1945.

medicinal soft soap and water for eight minutes and by washing in solutions of 1:1,000 zephiran chloride for three minutes. The solutions employed for chemical cleansing were zephiran chloride tincture (containing 50 per cent alcohol, U. S. P.), zephiran chloride tincture (containing 50 per cent alcohol, U. S. P., and 10 per cent acetone) and

TABLE 2.—*Bactericidal Effect of Soap and Water Plus Zephiran Chloride Tincture Without Acetone*

Results of Cultures after Scrubbing for Eight Minutes and Washing in 1:1,000 Zephiran Chloride Tincture Without Acetone for Three Minutes.

|         | Culture After<br>Preparation of the<br>Hands,<br>Number of Bacteria | After Gloves<br>Were Worn for<br>1 Hour,<br>Number of Bacteria | After Washing in<br>Zephiran Chloride<br>for 3 Minutes,<br>Number of Bacteria |
|---------|---|--|---|
| 1.....  | 1,000   | 23,600   | 300   |
| 2.....  | 9,600   | 80,000   | 400   |
| 3.....  | 300   | 17,600   | 1,300   |
| 4.....  | 300   | 24,000   | 400   |
| 5.....  | 45,000  | 172,000  | 56,000  |
| 6.....  | 3,200   | 26,000   | 15,100  |
| 7.....  | 7,100   | 129,600  | 1,700   |
| 8.....  | 300   | 1,400  | 100   |
| 9.....  | 4,100   | 4,700  | 700   |
| 10..... | Negative  | 35,200   | 16,500  |
| 11..... | 700   | 232,800  | 100   |
| 12..... | 100   | 25,600   | Negative  |
| 13..... | 400   | 1,100  | 100   |
| 14..... | 100   | 3,300  | 500   |
| 15..... | 6,400   | 49,600   | 1,100   |

TABLE 3.—*Bactericidal Effect of Soap and Water Plus Zephiran Chloride Tincture Containing Acetone*

Results of Cultures after Scrubbing for Eight Minutes and Washing in 1:1,000 Zephiran Chloride Tincture Containing 10 per Cent Acetone for Three Minutes.

|         | Culture After<br>Preparation of the<br>Hands,<br>Number of Bacteria | After Gloves<br>Were Worn for<br>1 Hour,<br>Number of Bacteria | After Washing in<br>Zephiran Chloride<br>for 3 Minutes,<br>Number of Bacteria |
|---------|---|--|---|
| 1.....  | 200   | 1,800  | 100   |
| 2.....  | 200   | 1,600  | 100   |
| 3.....  | 400   | 25,600   | 500   |
| 4.....  | 200   | 20,800   | Negative  |
| 5.....  | 500   | 300  | Negative  |
| 6.....  | 200   | 10,200   | 200   |
| 7.....  | 57,600  | Uncountable  | 7,600   |
| 8.....  | Negative  | 5,600  | 800   |
| 9.....  | 4,100   | 28,800   | Negative  |
| 10..... | 6,300   | 1,700  | 4,300   |
| 11..... | 1,100   | 5,800  | 4,700   |
| 12..... | 7,000   | 23,400   | 2,400   |
| 13..... | 4,200   | 11,800   | 6,600   |
| 14..... | 1,500   | 33,600   | 1,000   |
| 15..... | 12,200  | 9,600  | 3,400   |

aqueous solution of zephiran chloride. The results are listed in tables 2, 3 and 4 respectively. The best results were obtained when the aqueous solution was employed. Thirteen of the cultures, taken immediately after preparation of the hands, were negative for bacterial growth. Eight subjects had negative cultures after wearing gloves for one hour. Twelve cultures, taken after chemical cleansing had been

repeated, were negative for bacterial growth. All three cultures taken of 6 of the subjects were negative.

To determine the value of zephiran chloride as a detergent for use in mechanical cleansing, the hands and arms were scrubbed for eight

TABLE 4.—*Bactericidal Effect of Soap and Water Plus Aqueous Solution of Zephiran Chloride*

Results of Cultures after Scrubbing for Eight Minutes and Washing in 1:1,000 Aqueous Solution of Zephiran Chloride for Three Minutes.

|         | Culture After<br>Preparation of the<br>Hands,<br>Number of Bacteria | After Gloves<br>Were Worn for<br>1 Hour,<br>Number of Bacteria | After Washing in<br>Zephiran Chloride<br>for 3 Minutes,<br>Number of Bacteria |
|---------|---|--|---|
| 1.....  | Negative  | Negative   | Negative  |
| 2.....  | Negative  | 400  | Negative  |
| 3.....  | Negative  | Negative   | Negative  |
| 4.....  | Negative  | Negative   | 100   |
| 5.....  | Negative  | Negative   | 200   |
| 6.....  | Negative  | Negative   | Negative  |
| 7.....  | Negative  | 100  | Negative  |
| 8.....  | Negative  | 1,100  | Negative  |
| 9.....  | Negative  | Negative   | Negative  |
| 10..... | Negative  | Negative   | Negative  |
| 11..... | Negative  | 20,800   | 1,200   |
| 12..... | 600   | 256,000  | Negative  |
| 13..... | 100   | 1,100  | Negative  |
| 14..... | Negative  | 200  | Negative  |
| 15..... | Negative  | Negative   | Negative  |

TABLE 5.—*Bactericidal Effect of Scrubbing and Washing with Aqueous Solutions of Zephiran Chloride*

Results of Cultures after Scrubbing with 1:500 Aqueous Solution of Zephiran Chloride for Eight Minutes and Washing with 1:1,000 Aqueous Solution of Zephiran Chloride for Three Minutes.

|         | Culture After<br>Preparation of the<br>Hands,<br>Number of Bacteria | After Gloves<br>Were Worn for<br>1 Hour,<br>Number of Bacteria | After Washing with<br>1:1,000 Solution of<br>Zephiran Chloride<br>for 3 Minutes,<br>Number of Bacteria |
|---------|---|--|--|
| 1.....  | Negative  | 3,600  | 1,200  |
| 2.....  | 200   | 4,800  | 2,000  |
| 3.....  | 2,200   | 4,000  | 500  |
| 4.....  | 6,800   | 41,600   | 8,900  |
| 5.....  | 200   | 100  | 1,000  |
| 6.....  | 6,400   | 3,000  | 2,400  |
| 7.....  | 4,800   | 5,000  | 400  |
| 8.....  | 5,600   | 2,000  | 2,100  |
| 9.....  | 1,100   | 200  | 600  |
| 10..... | 1,800   | 800  | 800  |
| 11..... | Negative  | 200  | 500  |
| 12..... | Negative  | 3,400  | 700  |
| 13..... | Negative  | 4,600  | Negative   |
| 14..... | Negative  | 100  | 1,200  |
| 15..... | Negative  | 3,900  | 200  |

minutes with a 1 : 500 aqueous solution of zephiran chloride and then washed in a 1 : 1,000 aqueous solution of zephiran chloride for three minutes. The results are listed in table 5. They were not so satisfactory as those obtained when medicinal soft soap was used as a detergent.



Inasmuch as zephiran chloride is a cationic detergent and soap is an anionic detergent, soap should not be mixed with zephiran chloride. When the cutaneous surface is scrubbed with soap and water, it is difficult to remove all the soap. If the hands and arms are washed in a basin containing zephiran chloride after being scrubbed with soap and water, it is difficult to prevent the transfer of a small amount of the soap to the zephiran solution. To determine the practical importance of this, a basin containing two gallons (7.5 liters) of a 1:1,000 aqueous solution of zephiran chloride was placed in the operating room for use as a chemical cleansing agent following mechanical cleansing with soap and water. The solution was not changed during the day. The number of persons that used the solution for chemical cleansing was recorded. At the end of the day 5 subjects used this solution as a

TABLE 6.—*Bactericidal Effect of Soap and Water Plus Aqueous Solution of Zephiran Chloride*

Results Obtained after Scrubbing for Eight Minutes and Washing in 1:1,000 Aqueous Solution of Zephiran Chloride for Three Minutes, the Zephiran Being Previously Used All Day in the Operating Room Before Being Employed for These Experiments. Two Gallons (7.5 Liters) of the Zephiran Solution Was Placed in the Wash Basin at the Beginning of the Day.

|   |   | Culture After<br>Preparation of the<br>Hands,<br>Number of Bacteria | After Gloves<br>Were Worn for<br>1 Hour,<br>Number of Bacteria | After Washing in<br>Zephiran Chloride<br>for 3 Minutes,<br>Number of Bacteria |
|---|---|---|--|---|
| Zephiran chloride<br>previously used<br>by 29 persons | 1 | 500   | 400  | 500   |
|   | 2 | 800   | 9,400  | 800   |
|   | 3 | 5,400   | 50,000   | 3,500   |
|   | 4 | 3,200   | 22,400   | 3,600   |
|   | 5 | 200   | 3,700  | 500   |
| Zephiran chloride<br>previously used<br>by 42 persons | 1 | 1,100   | 168,400  | 1,100   |
|   | 2 | 1,300   | 35,400   | 1,200   |
|   | 3 | 20,800  | 320,000  | 7,600   |
|   | 4 | 2,300   | 35,200   | 800   |
|   | 5 | 700   | 3,200  | 1,000   |

chemical cleansing agent after scrubbing with soap and water for eight minutes. Cultures were taken immediately after preparation of the hands, after gloves had been worn for one hour and after chemical cleansing had been repeated following removal of the gloves. The results are listed in table 6. In both experiments the zephiran chloride was inactivated to such an extent that its bactericidal power was reduced. Although all the cultures were positive for bacterial growth, the results were as good as those obtained when fresh 70 per cent alcohol was employed.

#### COMMENT AND CONCLUSIONS

Zephiran chloride is a good chemical cleansing agent for use in the preoperative preparation of the hands and arms. In these experiments a 1:1,000 aqueous solution of zephiran chloride and 1:1,000 zephiran chloride tincture (containing 50 per cent alcohol, U. S. P., and 10 per cent acetone) proved to be better chemical cleansing agents

than 70 per cent alcohol. The results obtained with the aqueous solution were better than those achieved with the use of zephiran chloride tincture. The reason for this may be twofold: First, when the hands are washed in these solutions the film on the cutaneous surface appears to be more perceptible when the aqueous solution is employed, and, second, since the zephiran chloride tincture has greater penetrating power than the aqueous solution, contaminated sebaceous material may have been washed out of the pilonidal follicles onto the cutaneous surface and the bacteria remained viable because of the inability of the zephiran chloride to penetrate the sebaceous material and cause their death.

Soap proved to be a better detergent for mechanical cleansing of the hands and arms than aqueous solution of zephiran chloride. The best results were obtained when soap was used as a detergent for mechanical cleansing and a 1:1,000 aqueous solution of zephiran chloride was employed as the chemical cleansing agent. When these two substances are used for the preoperative preparation of the hands and arms, great care must be taken to remove the soap from the skin before chemical cleansing is performed. This is necessary because soap exerts an inactivating influence on zephiran. Most of the soap can be removed from the hands and arms by scrubbing with a clean brush in running tap water for one minute. When chemical cleansing is performed by washing of the hands and arms in a basin containing zephiran chloride this solution should be changed frequently. This problem may also be solved by applying the zephiran chloride to the hands and arms with a dispenser. When zephiran chloride is used as a chemical cleansing agent for the preoperative preparation of the hands, it is not necessary to scrub with soap and water between clean operations; flushing the hands and arms in running tap water to remove the powder and perspiration and then washing in a 1:1,000 solution of aqueous zephiran chloride for three minutes will be satisfactory.

Members of the operating room staff cooperated in these experiments.

## REPAIR OF DEFECTS OF THE SKULL

With Special Reference to the Periorbital Structures and Frontal Sinus

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CONSIDERABLE experimental and clinical evidence has accumulated to establish the biologically inert character of tantalum as an alloplastic material for the repair of defects of the skull. Pudenz<sup>1</sup> demonstrated the tolerance of brain tissue for tantalum clips and later showed the metal to be noncorrosive and nontoxic when used in the skull.<sup>2</sup> This has been substantiated by the work of others, notably, Carney,<sup>3</sup> Burke<sup>4</sup> and Fulcher.<sup>5</sup> In the past few years, several extensive reports on the use of this material in large series of cases have been published and the general principles and methods have been established. Woodhall and Spurling<sup>6</sup> and Robertson<sup>7</sup> have demonstrated its applicability in the repair of defects caused by war wounds, while Echols and Colcough<sup>8</sup> and Gardner<sup>9</sup> have employed it in the repair of defects such as are seen in civilian practice. In the latter instance, tantalum sheet metal has been extremely satisfactory in repair of the defects following operative treatment of osteomyelitis of the frontal bone and involvement of the calvarium by tumor and in other conditions in which the diseased bone must be removed.

The present consideration is of a specialized use of tantalum, namely, in the reconstruction of defects involving the frontal region, particu-

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1. Pudenz, R. H.: The Use of Tantalum Clips for Hemostasis in Neurosurgery, *Surgery* **12**:791-797 (Nov.) 1942.

2. Pudenz, R. H.: The Repair of Cranial Defects with Tantalum, *J. A. M. A.* **121**:478-481 (Feb. 13) 1943.

3. Carney, H. M.: An Experimental Study with Tantalum, *Proc. Soc. Exper. Biol. & Med.* **51**:147-148 (Oct.) 1942.

4. Burke, G. L.: The Corrosion of Metals in Tissues: An Introduction to Tantalum, *Canad. M. A. J.* **43**:125-128 (Aug.) 1940.

5. Fulcher, O. H.: Tantalum as a Metallic Implant to Repair Cranial Defects: A Preliminary Report, *J. A. M. A.* **121**:931-933 (March 20) 1943.

6. Woodhall, B., and Spurling, R. G.: Tantalum Cranioplasty for War Wounds of the Skull, *Ann. Surg.* **121**:649-671 (May) 1945.

7. Robertson, R. C. L.: Repair of Cranial Defects with Tantalum, *J. Neurosurg.* **1**:227-236 (July) 1944.

8. Echols, D. H., and Colcough, J. A.: Cranioplasty with Tantalum Plate, *Surgery* **17**:304-314 (Feb.) 1945.

9. Gardner, W. J.: Closure of Defects of the Skull with Tantalum, *Surg., Gynec. & Obst.* **80**:303-312 (March) 1945.

larly those in which the outer or both walls of the frontal sinus have been destroyed and in which the supraorbital ridges and orbital margin are included in the defect.

Small defects involving the supraorbital ridge or the frontotemporal angle of the forehead give rise to deformities which are out of proportion to the amount of bone loss. Surgical procedures on the frontal sinuses for the treatment of suppurative sinusitis frequently leave defects, the repair of which by autogenous plastic procedures is complicated and difficult. The radical removal of bone, which is necessary at times in the treatment of acute osteomyelitis of the frontal region, is particularly disfiguring. While it may be possible to retain much of the supraciliary arch in elective surgical procedures, this is not always so in the extensive comminuted fractures of the frontal region which result from vehicular accidents. The presence of a depressed area in the frontal region, where normally a convex surface exists, results in a distortion of the facial characteristics of a person. The contour of the frontal region is peculiar to each person, and care must be taken not only to preserve the vertical and lateral curvature but also to maintain the angle which exists between the frontal and temporal regions. This angle is formed in part by the lateral orbital wall, and a defect in this region results in a flattened appearance of the side of the head and undue prominence of the eye. This region is particularly important when the eye has been enucleated. The loss of the orbital fat pad (common in war wounds) and the tendency for the intraorbital tissues to retract necessitate reconstruction of the shelving portion of the supraorbital ridge as well as of the lateral orbital rim.

Prior to any detailed consideration of the various types of defects, the importance of countersinking the tantalum plate until it is level with the surface of the bone must be emphasized. Not only does this insure the best cosmetic result, but, it is my belief, repeated accumulation of fluid between the plate and the scalp is not infrequently caused by irritation from a plate which is insecurely anchored. In 1 known instance, fluid repeatedly accumulated after aspiration for several months in the occipital region where a tantalum plate had been loosely sutured to the pericranium. When the plate was removed there was no evidence of infection nor was the plate in any way adherent to the surrounding tissues. When small, well placed tantalum wedges driven into the diploic space are used, the position and immobility of the plate are insured. This is important in the frontal region, where frequently only the superior edge of the plate can be fastened.

It should also be emphasized at this time that the tantalum plate may be fashioned at the operating table and placed over a defect at the time of primary operation. While it may not be desirable to do this when there has been active acute infection, it is certainly feasible

and often desirable in the average traumatic wound. Tantalum itself causes no severe reaction in the presence of infection nor, as a foreign body, does it prevent healing in the presence of infection provided adequate drainage of the infected area is established and maintained before the formation of multiloculated pockets and walled-off areas under the plate. Should the latter be allowed to form, removal of the plate eventually may become necessary. The radical removal of infected bone in the treatment of sinusitis may be followed by tantalum cranioplasty to restore the cosmetic appearance,<sup>10</sup> and if all the diseased bone is removed and adequate drainage established through the nose the plate may be put in shortly after the primary operation. Whenever tantalum is used at the time of primary operation, the same care should be taken in fashioning of the plate and preservation of the contour of the frontal region as in the repair of any cosmetic defect.

#### I. DEFECTS INVOLVING THE LATERAL ORBITAL RIM

In this group are the defects in which the loss of bone often includes the zygomatic process of the frontal bone, either completely or partially. In the severe wounds which involve this lateral portion of the supra-ciliary arch, the upper portion of the frontal process of the zygomatic bone may be included in the defect. In few instances is the defect in the bone limited only to these structures, and there is almost always some loss of bone in the adjacent areas, including the frontal or temporal regions or both. As has been stated previously, the resulting deformity not only causes undue prominence of the eye but gives a flattened appearance of the side of the head. The deformity is frequently accentuated by loss of temporal muscle as a result of either tissue destruction from the injury itself or loss from necessary débridement of the wound. It is possible to a limited degree to compensate for soft tissue deformity by careful contouring of the tantalum plate, but as a general rule it is best to attempt to reconstruct only the pattern of the bone and to reserve soft tissue deformities for correction by other plastic procedures.

When the defect is small and underlies a relatively normal temporal muscle, there is no need to cover it with a plate. However, when the defect is large and particularly when the overlying muscle is thin and the area sunken, the plate for the orbital defect should be formed with an extension to underlie the temporal muscle. It must be remembered that the temporal fossa is deep and is concave, but when normally filled with muscle tends to have a moderately flat contour as compared with the convex surface of the frontal bone. In the final preparation of the plate at the operating table, this fronto-

10. Canfield, N., and others: Tantalum Implants for Skull Defects, *Proc. Roy. Soc. Med.* 38:293-298 (April) 1945.

temporal angle must be taken into account, particularly after the muscle has been stripped from its attachments. The anterior attachment of the temporal muscle at the superior temporal line, actually an upward and slightly posterior projection of the zygomatic process of the frontal bone, is the critical point in the reconstruction of this region. It has been the practice, whenever possible, to form the edge of the tantalum plate about the root of the zygomatic process to insure a proper contour. The following 2 cases are illustrations of defects such as have been discussed.

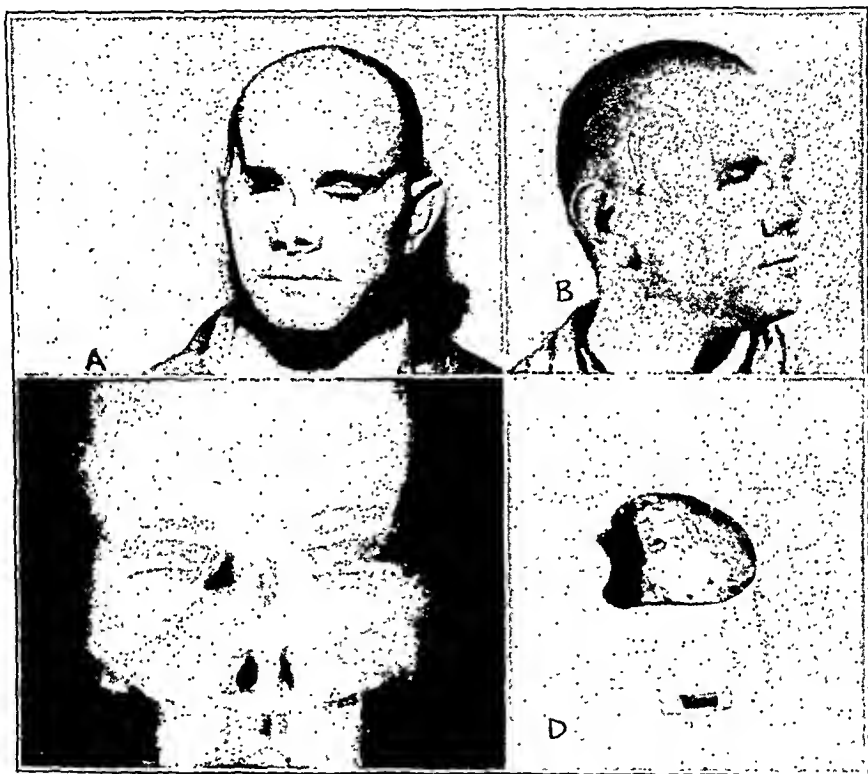


Fig. 1 (case 1).—*A*, preoperative photograph to show the defect in the lateral orbital wall and the temporal region. *B*, postoperative photograph to show the reconstruction of the lateral orbital rim. *C*, preoperative roentgenogram showing the absence of the lateral portion of the supraorbital ridge and lateral orbital rim. Roentgenogram was reversed in photography. *D*, tantalum plate. Note the contouring of the edge to form a shelf.

CASE 1.—A soldier was wounded when an enemy mine exploded on April 19, 1945. He received multiple wounds of the face, nose and head, with a penetrating wound of the right frontotemporal region, which destroyed the right eye. Traumatic cataract, with adhesions of the iris, developed in the left eye, and the patient was left with minimal vision. In preparation for further plastic procedures, the soldier was admitted to the hospital for reconstruction of the defect of the skull.

There was loss of bone in the right temporal region and at the lateral aspect of the orbital rim. The temporal muscle was extremely thin, and the area of the

defect was sunken (fig. 1 *A*). The extreme lateral portion of the supraorbital arch was missing, along with the corresponding portion of the orbital margin, and the zygomatic process was absent (fig. 1 *C*). The defect measured 5 cm. vertically and about the same horizontally.

A plate was fashioned which would adequately cover the defect under the temporal muscle as well as restore the missing portion of the orbital rim. Because adequate exposure could not be obtained through the irregular scar of the old incision, a small scalp flap was reflected in the temporal region, with the base placed anteriorly. It should be noted that a simple flat plate was not used but that a shelving portion which could be contoured about the remnant of the zygomatic process was utilized.

In this instance, the defect in the temporal region was such that the anterior edge of the plate formed the margin of the superior temporal line and the normal frontotemporal angle was restored (fig. 1 *B*).

CASE 2.—A soldier received a gutter type bullet wound in the right frontotemporal region on April 14, 1945, which resulted in extensive loss of bone. The defect involved a large portion of the squamous temporal region, the frontal bone, including the lateral two thirds of the supraorbital arch and zygomatic process, and the right frontal sinus (fig. 2 *C*). There was considerable depression of the temporal region, and the right globe appeared prominent, owing to destruction of the frontotemporal junction (fig. 2 *A*).

A large plate was fashioned which covered all portions of the defect. It was necessary to form a sharp angle between the frontal and temporal portions of the plate, and the exact amount of depression of the subtemporal portion of the plate was adjusted at the operating table (fig. 2 *D*). In this instance the posterior portion of the plate was not fastened with wedges, and it was necessary to do this at a second procedure because of excessive prominence of the temporal region due to "springing" of the free portion of the plate. The final result was one of restoration of both the frontal and the temporal contour, with the formation of a normal-appearing supraorbital ridge (fig. 2 *B*).

It was possible to obtain adequate exposure of the entire region through the original operative incision. This is usually the case, but occasionally it may be necessary to use another approach. When the approach is one of election, a concealed incision should be used when possible. This case illustrates the necessity of fastening the plate, particularly at points where there may be a tendency for the plate to "spring."

## II. DEFECTS INVOLVING THE SUPERIOR ORBITAL RIM, THE ANTERIOR ORBITAL PLATE AND THE FRONTAL SINUS

Whether the defect is confined to this anterior portion of the frontal bone or whether there is additional loss to include the frontal eminence, the problem of repair is essentially the same, namely, the restoration of a normally positioned and normally curved supraorbital arch. A second and equally important function of any plastic procedure in this region is the restoration of the anterior portion of the orbital plate when this is absent.

Injury to this region is often associated with damage to the orbital contents, frequently with destruction of the eye itself, and a common sequence is partial loss or shrinkage of the intraorbital contents. This eventually results in retraction of the overlying soft tissues, particularly of the upper eyelid. While this soft tissue deformity cannot be completely restored by the use of tantalum, the reconstruction of the anterior portion of the orbital roof by means of a shelving border to

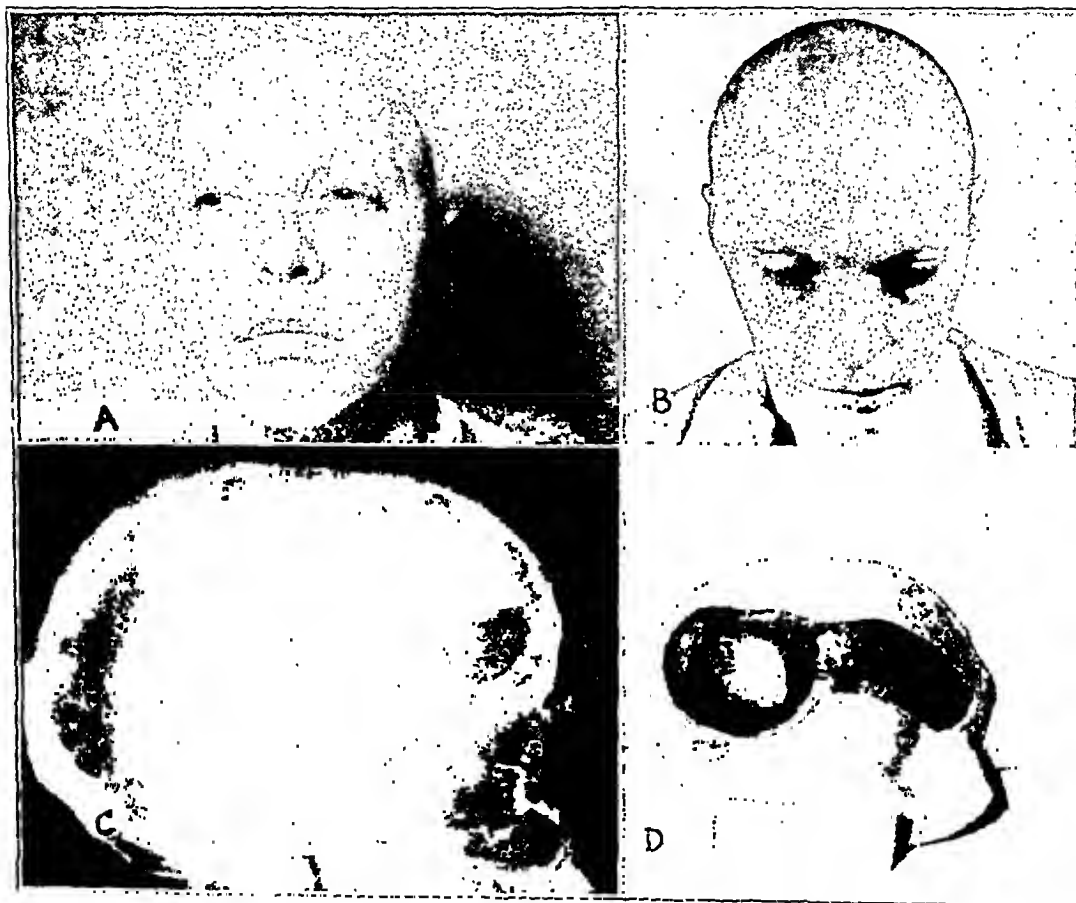


Fig. 2 (case 2).—*A*, preoperative photograph to show the deformity caused by the absence of the lateral half of the supraorbital ridge. Note the prominence of the eye. *B*, postoperative photograph showing the reconstruction of the supraorbital ridge and frontotemporal angle. *C*, lateral roentgenogram showing the extent of the defect, which involved both frontal and temporal regions. *D*, tantalum plate. Note the angle at the frontotemporal region and the depressed area to underlie the temporal muscle.

the tantalum plate can do much to lessen the deformity. In the formation of such a plate, there is a tendency to underestimate the degree of curvature, particularly since the curves must be present in two separate planes. The curve of the plate should be slightly overcom-



pensated to allow for the slight decrease in thickness, through scarring, of the overlying soft tissues.

The plate may be placed too high, and one must rely on available landmarks to determine the correct position. The newly formed ridge should conform as nearly as possible to that of the opposite side. When both ridges are absent or when the opposite one cannot be used as a landmark, the presence of a small amount of retained arch at either end is of considerable assistance. There is frequently considerable scar contracture of the upper eyelid, with the eyebrows being displaced downward and even into what remains of the upper lid. This scarring may be such as to prevent the placing of the plate low enough to correspond with the opposite side. After cranioplasty and the restoration of the normal convex surface, the displaced eyebrow may return to the normal position but often with shortening of the upper lid. For this reason, plastic procedures on the lids should not be undertaken until the bony contour has been restored. The substitution of the soft tissues of the supraciliary region for the upper lid may often be recognized by the presence of a portion of the eyebrow on what appears to be lid itself.

In the restoration of the ridge, it is not sufficient to obtain the proper position and lateral curve of the opposite side. There is considerable difference among persons, and in those with large frontal sinuses and prominent brows the most difficulty may be had in obtaining corresponding prominence of the ridge. The orbital margin is actually the most anterior extent of the orbital plate, and the positioning of the plate evenly with it will result in loss of the usual frontal prominence of the brow. It is not necessary to countersink that portion of the plate which is contiguous with the remnants of the supra-orbital ridge, but when sufficient of the latter structure is present the lower edge of the plate may be fastened with a small tantalum wedge.

In several cases an open frontal sinus has been exposed when the primary injury did not result in entire destruction of both walls. It has been the practice to make certain that no mucous membrane remains lining the cavity but to do nothing beyond that. There have been no infections which could be ascribed to exposure of the open sinus. The following cases illustrate the type and extent of the defects which have been discussed. While these cases are all cases of war injuries, they closely resemble those which are seen after accidents or surgical procedures in this region.

CASE 3.—A soldier received a compound, comminuted fracture of the left frontal region when he was struck by high explosive shell fragments on Feb. 6, 1945. The injury destroyed the left eye and shattered both walls of the frontal sinus and a portion of the roof of the orbit. At the time of admission for cranioplasty, examination disclosed the entire supraorbital ridge and the anterior portion of the orbital plate to be absent (fig. 3A). Except for a small bony prominence

situated laterally, there was nothing to indicate the normal position of the supra-ciliary arch. The medial half of the eyebrow was nearly in its normal position, but the lateral half was pulled down over the badly scarred and contracted tissues which formed the upper eyelid. The soft tissues in the region were all involved in the scar, adding to the deformity caused by the loss of bone.

A plate was fashioned, with a considerable shelving lower border, to correct the loss of bone from the orbital margin and anterior orbital roof (fig. 3 *D*). Because of the excessive prominence laterally, due to anterior displacement of

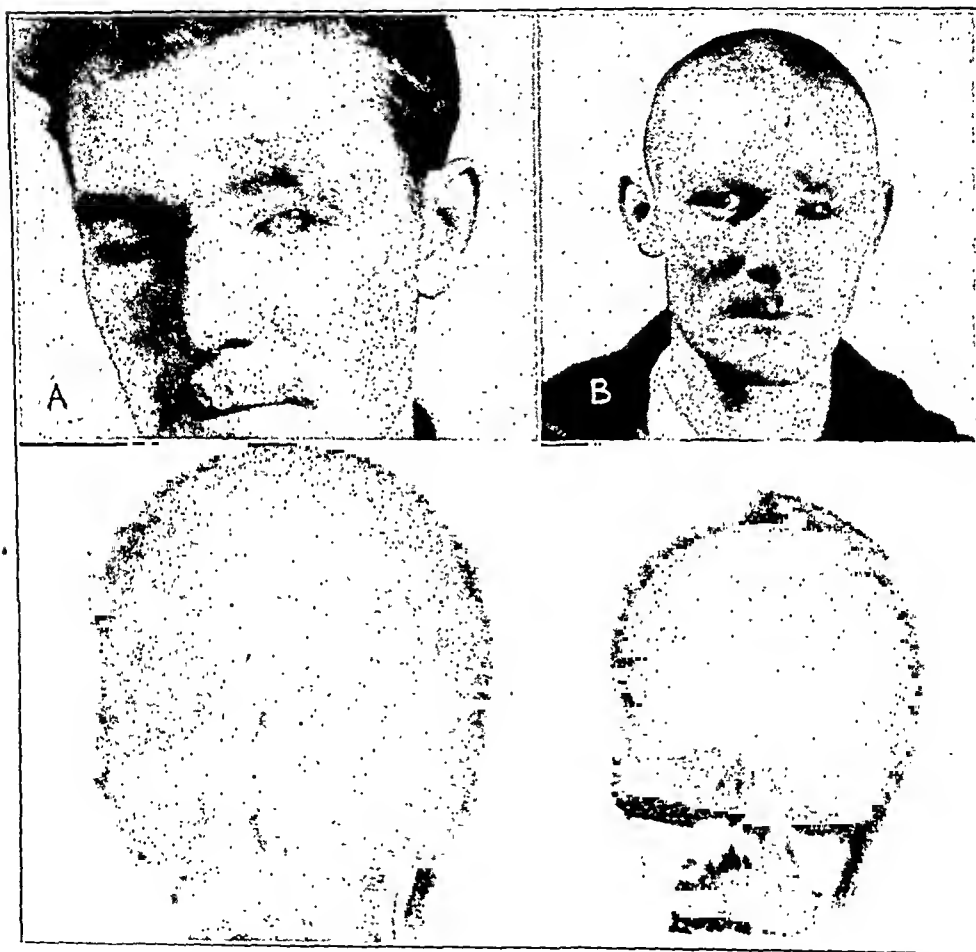


Fig. 3 (case 3).—*A*, preoperative photograph showing the absence of the left supraorbital ridge. Note the scar and retraction of the upper eyelid. *B*, postoperative photograph showing the reconstruction of the ridge. *C*, preoperative roentgenogram showing the complete absence of the supraorbital ridge and the anterior orbital plate. *D*, postoperative roentgenogram showing the position of the tantalum plate.

one of the bone fragments, it was impossible to obtain an even contour to the ridge. Accordingly, a ridge was formed to correspond to the normal position rather than to the displaced lateral angle. The badly scarred and shortened upper lid also interfered with the placing of the medial border of the plate as low as would have been desired. The superior margin of the defect was shelved to allow

the plate to lie evenly with the surface of the skull, and the plate was held in position by several wedges driven into the diploic space along the upper border.

Postoperatively, there was considerable improvement in the position of the displaced lateral half of the eyebrow. While a perfect supraorbital ridge was not obtained, there was much improvement over the preoperative appearance and there was formed a structure on which further plastic procedures could be carried out on the soft tissues (fig. 3*B*). During the operation, the anterior portion of what remained of the right frontal sinus was exposed. The sinus was free of mucous membrane, and nothing further was done to it.

This case illustrates the difficulties which may be encountered when there is excessive scarring of the soft tissues and displacement of the bone structures surrounding the defect. The necessity for an adequate exposure and the severity of the local scar precluded use of the original incision, and a frontal scalp flap, with most of the incision concealed behind the hair line, was used.

CASE 4.—A soldier was injured in a motorcycle accident in Germany on June 28, 1945, in which he sustained a compound, comminuted and depressed fracture of the left frontal region, with penetration of the dura and brain. At the time of primary operation, a left frontal scalp flap was reflected and the depressed fragments of bone removed. The fracture included both walls of the frontal sinus and a portion of the anterior aspect of the orbital plate.

At the time of admission there was a pulsating, oval defect in the left frontal region, which measured 6.5 by 4.5 cm. The supraorbital ridge was absent except for its lowermost edge and a small remnant of bone which could be palpated above the outer canthus of the eye (fig. 4*A*).

The operative area was approached through the scar of the previous incision. There was some thinning of the bone edges, and the plate was allowed to overlap sufficiently to cover the thinned area. A plate had been fashioned with a shelved lower border to compensate for the defect in the orbital plate, and at the time of operation this border was adjusted to correspond with the plane of the remaining bone forming the orbital roof. Postoperatively, there was excellent restoration of the contour of the brow and forehead (fig. 4*B*).

In addition to the destruction of the supraorbital ridge there was a considerable defect involving the region of the frontal eminence, and this necessitated careful contouring of the upper portion of the plate. In the process of exposing the defect, the scalp must be dissected from the underlying dura. Usually a fairly distinct cleavage plane may be found between the two structures, but if the defect is of long standing or if there has been intercurrent infection scar tissue may make the dissection difficult. If the dura is inadvertently opened, it should be closed with several interrupted fine silk sutures.

In extensive bifrontal injuries there is often destruction of the glabella and frequently of the upper portion of the nasal bridge as well. In such instances a plate can be formed which includes the upper portion of the nasal bridge. If there is only a small defect in the nasal bridge, a coronal incision may be used and the operative site exposed by reflection of the scalp forward. However, if the nasal defect is

large or if the soft tissues are severely scarred and adherent in this region, it may be difficult to expose the upper edge of the nasal bone through such an incision. If the nasal defect is to be repaired, it may be best in some cases to approach the operative site through an incision which passes through the region of both eyebrows and across the nasal bridge. Great care must be exercised not to enter the nasal cavity in the dissection, and the edge of the tantalum plate must fit perfectly with the upper edge of the nasal bone or an unsightly elevation will result.

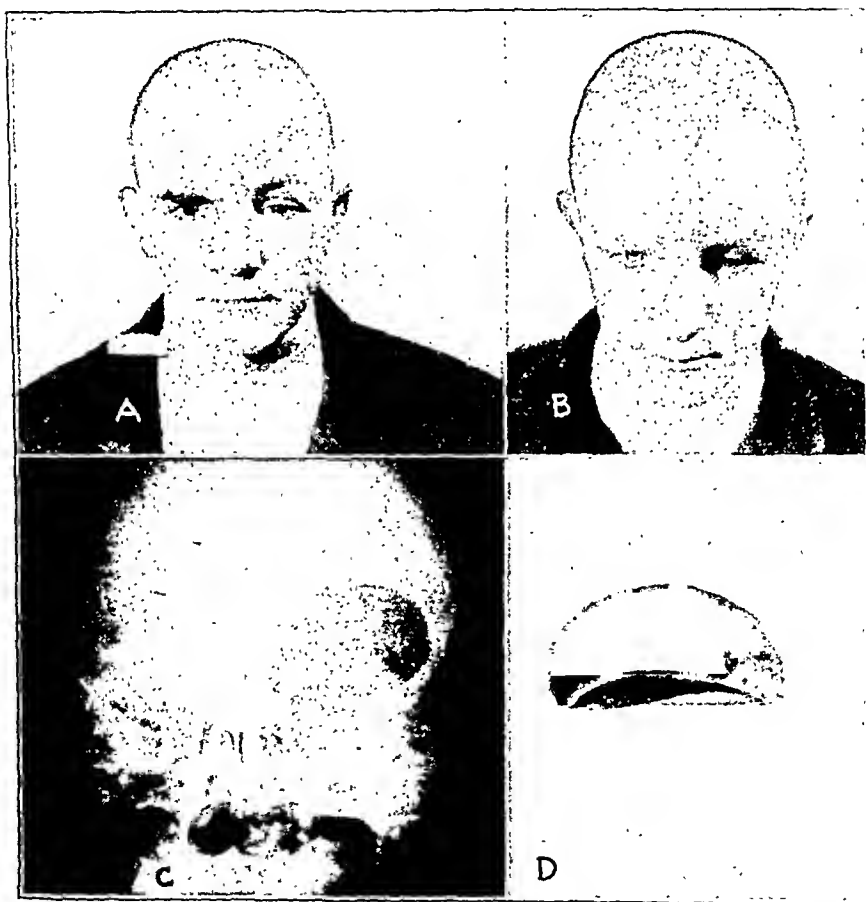


Fig. 4 (case 4).—*A*, preoperative photograph showing defect involving the frontal region and part of the supraorbital ridge. *B*, postoperative photograph. Note the presence of the formed ridge and normal frontal contour. *C*, preoperative roentgenogram showing the absence of a portion of the ridge. *D*, tantalum plate. Note shelving of a portion of the lower border to replace orbital margin.

### III. EXTENSIVE DEFECT OF THE CONVEXITY INVOLVING ONE OR BOTH SIDES

Traumatic defects involving one or both sides are for the most part confined to those resulting from war wounds but are occasionally

seen in civilian practice as results of automobile accidents, high velocity missiles, with a bursting type of fracture, and industrial injuries. They are somewhat more frequently seen, however, as results of necessary surgical removal of bone in the treatment of such conditions as acute fulminating osteomyelitis of the frontal region or infiltration of the skull by neoplasms arising either locally or in the adjacent tissues.

The difficulty in obtaining the proper contour of the frontal region depends to some extent on the prominence of the frontal sinuses and the development of the frontal eminences. In these large plates it is particularly important that the amount of curvature be overcorrected to some degree. In fashioning the plate before operation, the impression is made after the defect has been filled in with dental wax. The contour obtained does not allow for the thickness of the soft tissues, and if the convexity is not increased moderately the forehead will appear flat after the plate has been placed. Even in these large plates, it has been the practice to shelve the edge of the bone sufficiently to allow the plate to rest evenly with the surface of the skull.

The exposure must be adequate, and, for these large defects, a concealed coronal incision or unilateral frontal flap passing back of the hair line is usually necessary. The scalp is reflected forward subperiosteally and dissected from the underlying dura. The dead space may be lessened and oozing from the dural surface discouraged by the use of several silk or tantalum wire sutures passed through the dura and fastened to the holes in the plate. It is important that careful hemostasis be obtained to prevent collections of fluid and blood beneath the plate, which might cause extradural compression of the brain. The following 2 cases illustrate the restoration which may be obtained after extensive and highly deforming injuries.

CASE 5.—The patient was a soldier admitted to the hospital for repair of a large defect of the frontal and anterior parietal skull secondary to a perforating gunshot wound sustained Feb. 5, 1945. There had been extensive loss of soft tissue at the time of injury, and several plastic procedures were necessary to obtain healing of the wound. At the time of admission there was a large sunken defect, which measured 12 by 12 cm. (fig. 5*A*). It involved almost the entire frontal region, extending to the superior temporal line on the right and to the midline of the orbit on the left. Superiorly, it reached the coronal suture. The supraorbital ridge was spared on the right, but the upper portion of the ridge was missing on the left.

Prior to operation a large plate was fashioned from an impression taken after the defect had been built up with dental wax. Because of the retained lower portion of the supraorbital ridge on the left, it was not necessary to shelve the lower border of the plate on this side. The defect was exposed through a coronal incision and the scalp reflected forward from the adherent dura. The dead space was reduced by a number of sutures passing from the dura to the holes in the plate. The plate was fastened to the shelved margin of the bone in the usual manner, with several tantalum wedges (fig. 5*D*).

Postoperatively, there was complete restoration of the frontal contour, with no deformity other than that of the soft tissue scar in the right frontotemporal region at the point of entrance of the missile (fig. 5 *B*).

In the preparation of the plate, the general rule has been to correct the contours and curves prior to operation and to adjust the final size at the time of operation. The plate, when prepared from the impression, is usually made somewhat oversized. Before operation it is fitted to the defect and shaped so as to present no sharp angles or prominences which may serve as points of irritation to the overlying scalp. At this

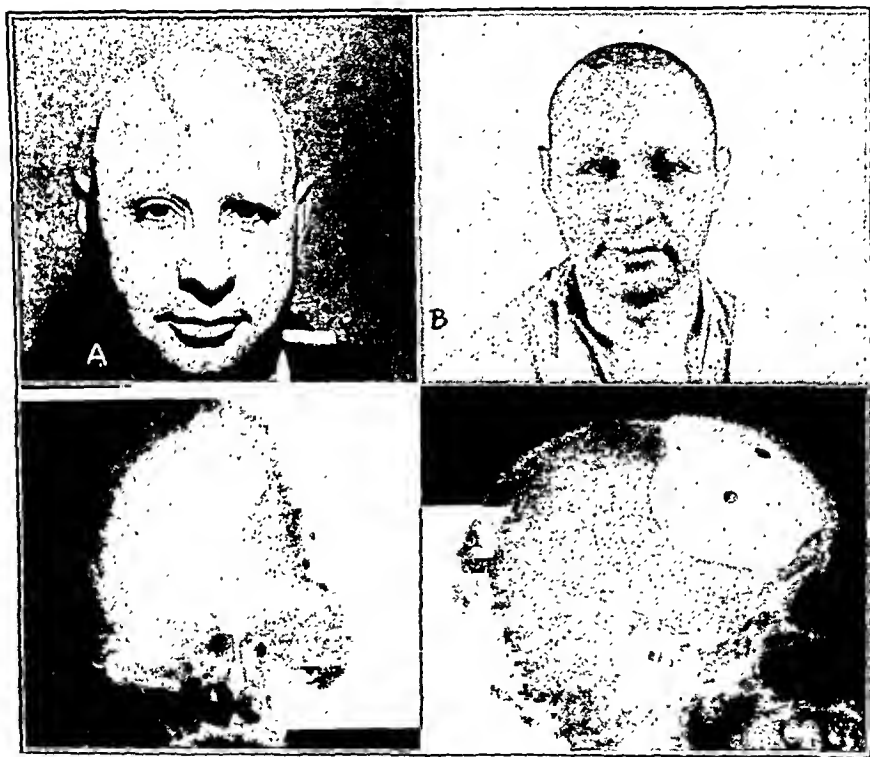


Fig. 5 (case 5).—*A*, preoperative photograph to show the large, sunken right frontal defect. Note that the major portion of the ridge is spared. *B*, postoperative photograph showing the restoration of the contour of the frontal region. *C*, preoperative roentgenogram showing extent of the defect. Note the presence of tantalum wire sutures at site of dural graft. *D*, postoperative roentgenogram showing the position of tantalum plate.

time, obvious excess of plate is removed and small but important changes are made in the contour. It is frequently necessary to increase the angle between the vertical and the shelving portions of plates for the supraorbital region. In the present case, it was necessary to increase the prominence of the frontal eminences, and this was done with the use of a ball-peen machinist's hammer and a hollowed block of wood. These plus straight and curved dental pliers and heavy

scissors suitable for cutting tantalum sheet metal should be included in the sterile set-up for any cranioplasty with tantalum.

CASE 6.—A soldier was wounded on Jan. 23, 1945, by a shell fragment which entered the right frontal region. There was extensive comminution of the bone and penetration of the dura and brain. After the primary operation, the wound became infected and a draining sinus developed in the left frontal region. On April 20, 1945, a scalp flap was reflected and a large extradural abscess drained. The wound healed without further complication, and repeated roentgenograms of the skull disclosed no evidence of infection of the bone.

There was a large defect, which measured 9 by 8.5 cm. and extended laterally from the midline to include the anterior third of the temporal region (fig. 6 C).

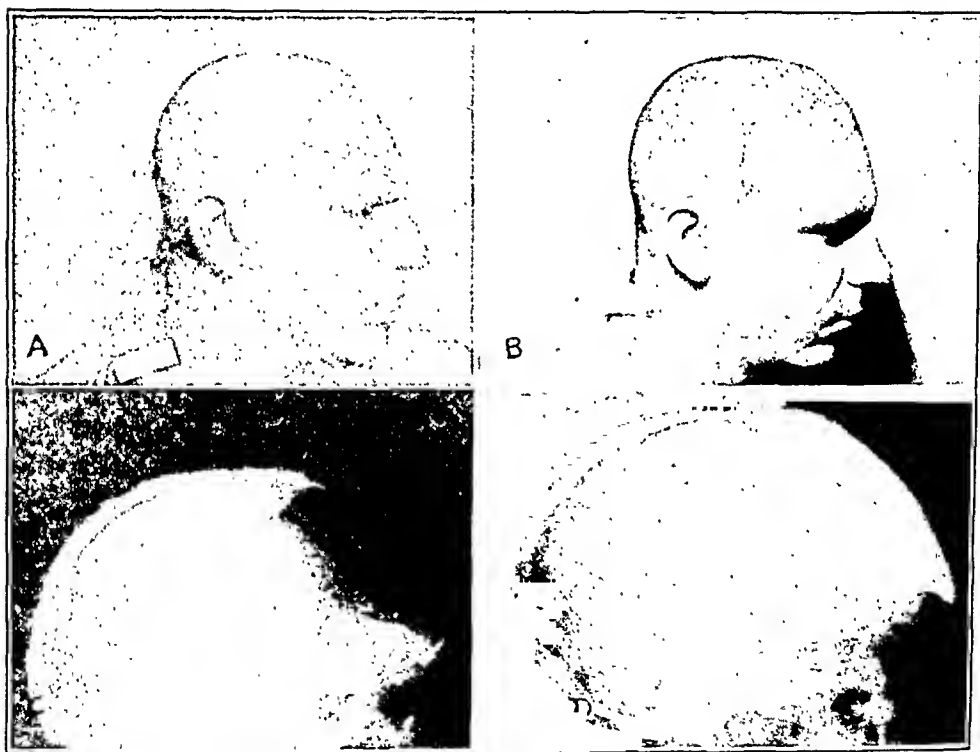


Fig. 6 (case 6).—A, preoperative photograph showing extensive bifrontal defect. B, postoperative photograph showing restoration of frontal contour and concealed incision. C, preoperative roentgenogram showing extent of bone loss. D, postoperative roentgenogram showing position of tantalum plate. Note anterior extent of plate to preserve supraorbital contour.

The supraorbital ridge was intact. The defect was sunken, and the scalp seemed adherent to the underlying dura (fig. 6 A).

A large plate was fashioned which appeared to reconstruct the contour of the frontal region. The entire defect of the bone was shelved and the plate fastened with tantalum wedges (fig. 6 B). Following operation there was some flattening of the forehead, which it seemed desirable to have corrected. Consequently, about six days later the plate was removed and reshaped at the operating table. The subsequent result was one of complete restoration of the normal shape of the head (fig. 6 B).

It may be necessary occasionally to remove a plate and adjust the contour if the first operation does not give the maximum cosmetic result. This is a relatively simple procedure, since the time-consuming part of the operation, the dissection of the scalp from the dura and the shelving of the bone edge, has already been carried out. In this case, as in several others, the dura was opened and the site of cortical injury explored. As a rule, prior to cranioplasty all bone fragments retained in the cerebral substance are removed, or where there has been considerable scar formation the scar is excised. It is emphasized that tantalum cranioplasty need not be considered as a separate procedure but can

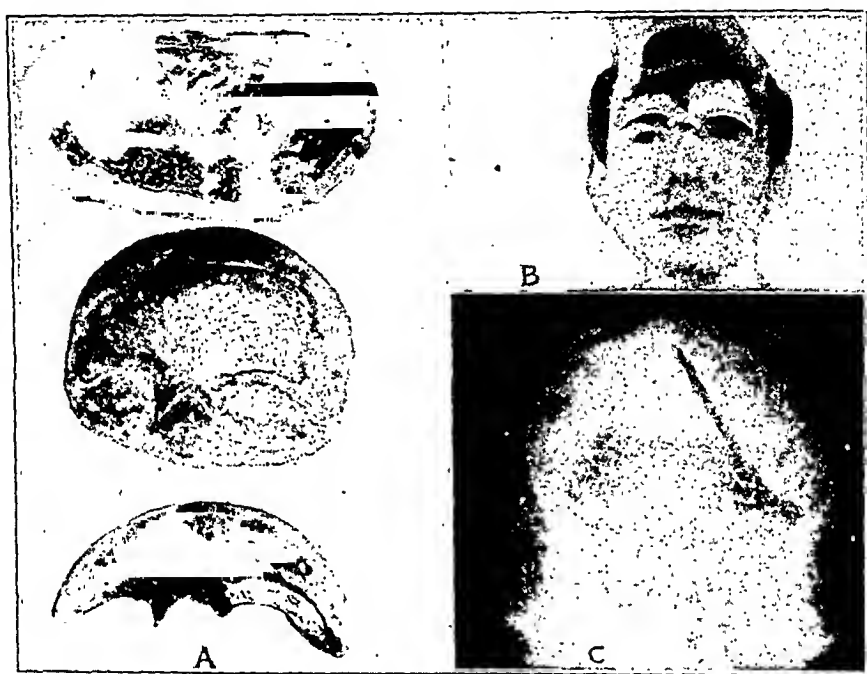


Fig. 7.—*A*, photograph showing metal molds used to form plates with complex curves. *B*, method of fitting plate over defect preoperatively to adjust contour. Note extension from glabella to correct defect of nasal bridge. *C*, roentgenogram showing type of defect requiring restoration of both supraorbital ridges, both orbital plates and bridge of nose.

be carried out as the final stage in any operation which may result in or which involves a disfiguring defect of the skull.

It has been the practice to precede the cranioplasty with a pneumoencephalogram when there is any indication that the underlying cerebral substance has been scarred. Under such conditions, excision of the scar is done and the cranioplasty carried out as an adjunct to this procedure. In several instances distinct improvement in speech defects and subjective symptoms has followed a simple cranioplasty. It is suggested that this is due to relief from the weight and traction of



the sunken and adherent scalp which eventually comes to inhibit the normal pulsations of the brain in the area of the defect.

In the repair of small defects of relatively long standing, it is sometimes necessary to have the plate overlap the edges of the bone for a distance of 1 cm. or more. This is due to the tendency for thinning of the bone edge to occur, and if the usual 2 to 3 mm. ledge for the plate is made in such an instance the entire area of repair will appear somewhat depressed.

#### SUMMARY

Special consideration has been given to the use of tantalum in the repair of defects of the skull which involve the supraorbital ridge, the orbital rim and plate and the adjacent bony structures. Emphasis has been placed on the restoration of the normal contour of the brow and forehead in relation to the anatomic structure of the supraciliary arch and orbital rim. It has been pointed out that reconstruction of the bony framework not only may serve as the basis for further plastic procedures on the soft tissues but may also prevent the development of unsightly cosmetic defects through the retraction of the orbital contents and soft tissues. Details of formation and adjustment of the tantalum plate to give the maximum cosmetic result have been discussed.

Col. R. Glen Spurling, Medical Corps, Army of the United States, gave suggestions which aided considerably in the preparation of this paper.

# CHEMOSURGICAL TREATMENT OF CANCER OF THE NOSE

## A Microscopically Controlled Method

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THE term "chemosurgery" was coined to designate a newly developed method for the microscopically controlled excision of certain accessible forms of cancer. The "chemo" portion of the term indicates that the tissues are chemically treated, while the "surgery" portion indicates that the tissues so treated are surgically excised. It is unfortunate, perhaps, that the term omits mention of the thorough microscopic control of excision afforded by the technic, because this control is the most important and only entirely new feature of the method.

The development of the method by experiments on animals<sup>1</sup> and the use of the method in the treatment of various accessible forms of cancer have previously been described.<sup>2</sup> The present article concerns the chemosurgical treatment of cancer of the nose, including the therapeutic results, in a series of two hundred and forty-three lesions treated over a nine year period.

### TECHNIC

The chemosurgical technic as applied to the treatment of cancer of the nose will be described by the presentation of the case of the patient pictured in figure 1.

The lesion had begun eight years previously as a crusted ulcer on the lower part of the bridge of the nose, just to the right of the midline. After having been treated three times by means of electrodesiccation and about fifty times by means of roentgen rays over a period of six years, the patient was referred for chemosurgical excision because of continued spread of the basal cell carcinoma. The entire left ala was atrophic, and a hole 3 mm. in diameter entered the nasal cavity in the

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From the Department of Surgery, Dr. E. R. Schmidt, chief, State of Wisconsin General Hospital, and the McArdle Memorial Laboratory for Cancer Research.

1. Mohs, F. E., and Guyer, M. F.: Pre-Excisional Fixation of Tissues in the Treatment of Cancer in Rats, *Cancer Research* 1:49 (Jan.) 1941.

2. Mohs, F. E.: Chemosurgery: A Microscopically Controlled Method of Cancer Excision, *Arch. Surg.* 42:279 (Feb.) 1941; Chemosurgical Treatment of Cancer of the Lip: A Microscopically Controlled Method of Excision, *ibid.* 48:478 (June) 1944.

region of the nasofacial sulcus (fig. 1 *A*). There was slight ulceration in the latter region, surrounded by a small amount of visible, pearly, carcinomatous tissue extending onto the ala. Palpation was valueless in detection of the extent of the carcinoma, because the scar tissue and also the fibrocartilaginous structure of the nose were similar to the cancer in consistency.

One-half hour after preparation with 0.03 Gm. of codeine and 0.65 Gm. of acetylsalicylic acid, the portion of the ala which was fairly definitely cancerous was given an application of dichloroacetic acid. When the skin turned white, indicating permeation through the keratin, the first application of zinc chloride fixative Z-108a<sup>3</sup> was made in an even thickness of about 0.5 mm. The fixative was covered with a thin cotton dressing, which in turn was covered by an overlapping cotton dressing spread with petrolatum to form a moisture-tight closure.



Fig. 1.—*A*, basal cell carcinoma of group C (average diameter, 3 to 4 cm.). Starting on the bridge of the nose, it had repeatedly recurred after three electrodesiccations and fifty roentgen ray treatments over a period of eight years. It was excised in six microscopically controlled stages by the chemosurgical technic (see figure 2). *B*, appearance of the lesion after separation of the final layer of fixed tissue. *C*, after healing. The patient had a plastic repair and is free of cancer after six years.

Adhesive tape was accurately applied to hold the dressing firmly in place. The analgesics previously mentioned were prescribed, with instructions to take them as often as every three hours, as needed. The patient was treated as an outpatient.

On the next day a layer of fixed tissue, 1.5 mm. in thickness, was excised with a scalpel. There was no pain or bleeding from this operation because the incisions were made through killed and fixed tissue. Since it was impossible grossly to visualize the cancer in the heavily scarred

3. This fixative paste contains 40 Gm. of stibnite (80 mesh sieve), 10 Gm. of powdered sanguinaria and 34.5 cc. of a saturated solution of zinc chloride.

tissue, the entire area was divided into six specimens so that a systematic microscopic search for the cancer could be carried out. The specimens were mapped on the white, fixed tissue of the lesion (merbromin being used) and on a pad of paper (fig. 2 A). The edges of the specimens were marked with merbromin and india ink for orientation (represented by straight and wavy lines respectively on the maps). Frozen sections were cut through the under surface of the specimens, which were examined under the microscope, and the areas of cancer marked on the paper map with red pencil (stippled in the accompanying diagrams). Since

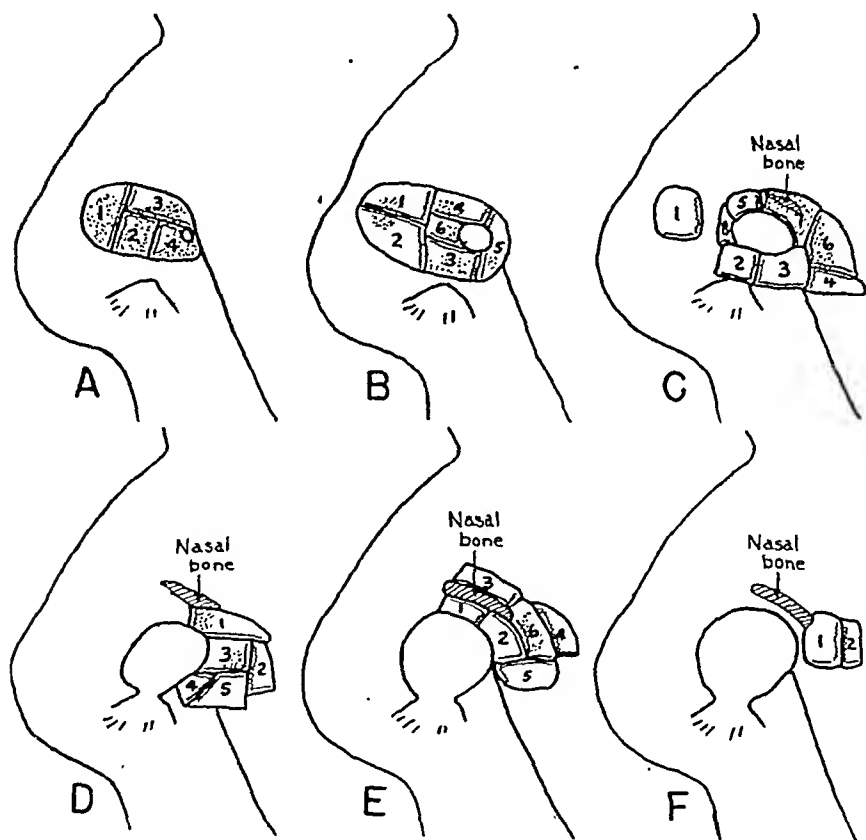


Fig. 2.—Maps showing locations of specimens removed on successive days from the lesion pictured in figure 1. Stippled areas represent cancer located by the microscopic examination of frozen sections made through the under surface of each specimen.

the area proved to be almost completely involved by basal cell carcinoma, the fixative was reapplied to the entire area in a thickness of about 0.5 mm.

The next day a second layer was excised and the areas of cancer located on a map (fig. 2 B). Since at this level some cancer-free areas were encountered, the application of fixative was limited to the cancerous portions of the lesion.

The third excision revealed that the remaining cancer was localized to the tissues internal and external to the nasal bone and to the region of the nasofacial junction. Further treatment was confined to these cancerous areas (figs. 2 *C* and 2 *D*), and two days later the tissues on the mucosal and cutaneous sides of the nasal bone became free of cancer (fig. 2 *E*). The last extension, which had eroded rather deeply along the embryologic fusion plane between the nose and the cheek, was eradicated on the following day (fig. 2 *F*).

When a cancer-free plane was reached, the lesion was covered with a petrolatum gauze dressing. Four days after the last application of fixative the remaining thin layer of fixed tissue was loose, so it could easily be removed with sharp-pointed scissors, revealing well vascularized granulation tissue (fig. 1 *B*). (The average time for separation of fixed tissue from the nose is 6.8 days, with limits extending from three to ten days.) The wound then was dressed three times a week with scarlet red gauze. The necrotic portion of the nasal bone was excised one week later, and by one week after that the wound was healed. The patient kept the defect (fig. 1 *C*) covered with adhesive tape, and one year later she was referred for a plastic repair, which was accomplished without complications and with excellent cosmetic results. There has been no evidence of recurrence after six years.

It will be noted that from the beginning of treatment the lesion described required a daily microscopic check on progress. This was due to the fact that the cancer tissue was not grossly distinguishable from the tissues of the nose, which were heavily scarred by previous treatment. Frequently, however, solid masses of cancer may be grossly detected by their grayish white color and cheesy consistency. Where cancer is so evidenced sections are unnecessary, but as soon as any doubt arises as to the nature of tissues sectioning should be instituted. Treatment should not be considered complete until cancer-free sections have been obtained from the entire area.

For lesions on the septum or inside the nose the technic is essentially as previously described, but with special attention to packing for restraining of secretions and holding of the dressings in place. In some instances in which mucous secretion is troublesome, fixative-impregnated gauze may be applied in place of the paste, which would be too rapidly carried away by the secretions. This gauze is prepared by the rubbing of some of the fixative paste into the meshes of cheesecloth and cutting to the desired size.

If bone or cartilage is involved, it is usually grossly evident as treatment proceeds. Fixation and excision are feasible in these tissues as well as in soft tissues except that, in the case of bone, rongeurs and chisels are used in place of the scalpel. Of course, frozen sections of bone cannot be made without the delay of decalcification, but areas of

eroding tissue may be removed and sectioned to determine whether the erosion is due to cancer or other causes.

Hemorrhage was rarely a problem because there are no large vessels in the nasal region. A few patients with hypertension had some bleeding from the angular artery during the separation of the final layer of fixed tissue from around the nasal tip. Though the bleeding usually stops spontaneously within a few minutes, it may be avoided by simply placing a suture-ligature around the vessel, which is located by its pulsation.

#### THERAPEUTIC RESULTS IN CASES OF BASAL CELL CARCINOMA OF THE NOSE

A total of two hundred and ten basal cell carcinomas of the nose were chemosurgically treated in the nine year period ending May 1, 1945, which date is seven months prior to this writing. The lesions were in all stages, from early to extremely advanced. More than one third of the patients had received unsuccessful surgical or irradiation treatment elsewhere. No instance of metastasis was observed.

*End Results After Six Months or More.*—While end results after six months are of limited value in comparison of the chemosurgical method with other methods, they come within a few per cent of the ultimate rate of cure. This is so because residual cancer, if left after chemosurgical treatment, usually makes itself evident within a six month period because it is not buried deep in a surgical incision nor is it kept in check by a dense radiation scar.

The 210 cases were divided into "indeterminate" and "determinate" groups, after the example of Martin, MacComb and Blady.<sup>4</sup> The indeterminate group is composed of 8 cases in which the patients died of intercurrent disease without evidence of recurrence or were lost track of without recurrence. The determinate group is made up of 202 cases in which unsuccessful results were obtained (the patients have died of cancer, have been lost from observation with cancer or are living with cancer) and those in which successful results were obtained (the patients who have been free of cancer for six months or more).

In the 202 cases of the determinate group the rate of cure after six months or more was 98 per cent (table 1).

*Three Year and Five Year End Results.*—An intensive follow-up program had as its aim the observation of every patient for at least five years. Of course, there were a number of deaths before the elapse of that period, due to the preponderance of elderly people in this series. Every effort was made to determine whether or not cancer was present at the time of death. The efficiency of the follow-up system is attested to by the fact that only 5 patients were lost from observation.

4. Martin, H. E.; MacComb, W. S., and Blady, J. V.: Cancer of the Lip, *Ann. Surg.* **114**:341 (Sept.) 1941.

In the three year period, successful results were obtained in 97.2 per cent of the 109 cases in the determinate group (table 1).

In the five year period, successful results were obtained in 94.3 per cent of the 53 cases in the determinate group (table 1).

TABLE 1.—*End Results for Basal Cell Carcinoma of the Nose After Periods of Six Months, Three Years and Five Years*

This series includes the cases of all patients with histologically proved basal cell carcinomas, both early and advanced, previously untreated and recurrent, who were admitted to the chemo-surgery clinic from July 31, 1936 to April 25, 1945 for the six month group; from July 31, 1936 to Oct. 12, 1942 for the three year group, and from July 31, 1936 to Oct. 4, 1940 for the five year group.

|  | Six<br>Month<br>Period | Three<br>Year<br>Period | Five<br>Year<br>Period |
|--|------------------------|-------------------------|------------------------|
| Total number of cases.....   | 210                    | 132                     | 50                     |
| Indeterminate group  |                        |                         |                        |
| Patients without recurrence dead from other causes.....  | 6                      | 21                      | 24                     |
| Patients without recurrence lost from observation.....   | 2                      | 2                       | 3                      |
| Total number .....   | 8                      | 23                      | 27                     |
| Determinate group  |                        |                         |                        |
| Total number .....   | 202                    | 109                     | 53                     |
| Unsuccessful results   |                        |                         |                        |
| Patients dead as a result of cancer.....   | 4                      | 3                       | 3                      |
| Patients with cancer lost from observation.....  | 0                      | 0                       | 0                      |
| Patients with cancer living.....   | 0                      | 0                       | 0                      |
| Total number .....   | 4                      | 3                       | 3                      |
| Successful results   |                        |                         |                        |
| Patients free from cancer for six month or more.....   | 198                    |                         |                        |
| Patients free from cancer for three years or more.....   | ...                    | 106                     |                        |
| Patients free from cancer for five years or more.....  | ...                    | ...                     | 50                     |
| Six month end results  |                        |                         |                        |
| Total number of cases with successful results divided by total number of determinate cases ( $198 \div 202$ )..... | 98%                    |                         |                        |
| Three year end results   |                        |                         |                        |
| Total number of cases with successful results divided by total number of determinate cases ( $106 \div 109$ )..... | ...                    | 97.2%                   |                        |
| Five year end results  |                        |                         |                        |
| Total number of cases with successful results divided by total number of determinate cases ( $50 \div 53$ ).....   | ...                    | ...                     | 94.3%                  |

*Effect of Size of Lesion on Prognosis.*—In the 202 cases in the determinate group in the six month period, the lesions were divided into four groups, according to their average diameter: A, under 1 cm. (fig. 3); B, 1 to 2 cm. (fig. 4); C, 2 to 3 cm. (figs. 1, 5, 6 and 7) and D, 3 cm. or more (figs. 8, 9 and 10).

TABLE 2.—*Effect of Size of Basal Cell Carcinoma on Prognosis*

| Group           | Average<br>Diameter,<br>Cm. | Number<br>of<br>Lesions | Successful Results |          |
|-----------------|-----------------------------|-------------------------|--------------------|----------|
|                 |                             |                         | Number             | Per Cent |
| A.....          | Under 1                     | 86                      | 86                 | 100      |
| B.....          | 1-2                         | 70                      | 70                 | 100      |
| C.....          | 2-3                         | 22                      | 22                 | 100      |
| D.....          | 3 or more                   | 24                      | 20                 | 83.3     |
| All groups..... |                             | 202                     | 198                | 98       |

The end results after a period of six months or more show that there were no failures in groups A, B and C and that the four failures of the entire series were in group D (table 2). As a matter of fact, each of the 4 patients in whom unsuccessful results were obtained had

lost most or all of his nose and had been treated for years by other methods before reporting to the chemosurgery clinic. Treatment in these cases was stopped at an optimum palliative level when it became evident that invasion was so extensive that a repair of the necessary defect would be impractical, in consideration of the age and physical condition of the patients.

It will be noted that even in group D successful results were obtained in 83.3 per cent of the cases. Many of the lesions in this group were



Fig. 3.—*A*, basal cell carcinoma of group A (under 1 cm.). It had recurred after three radium and two electrodesiccation treatments. Microscopic sections revealed a shelflike extension of the neoplasm under the scar superior to the crusted ulcer. The insert shows a reconstruction of the cancer, the actual extent of which was much greater than the small visible portion at the lower end. *B*, healed lesion. The patient is free of cancer after six years.

beyond any reasonable hope of cure by the usual surgical or irradiation technics.

*Effect of Previous Treatment on Prognosis.*—In the 202 cases in the determinate group in which basal cell carcinomas were chemosur-

TABLE 3.—*Effect of Previous Unsuccessful Treatment of Basal Cell Carcinoma on Prognosis*

|                           | Number of Patients | Successful Results |          |
|---------------------------|--------------------|--------------------|----------|
|                           |                    | Number             | Per Cent |
| Previously treated.....   | 73                 | 69                 | 94.5     |
| Previously untreated..... | 129                | 129                | 100      |

gically excised, seventy-three of the lesions (36.1 per cent) had previously been unsuccessfully treated by surgical operation, roentgen ray, radium or caustics, either alone or in combination. Although it was possible to salvage 69 (94.5 per cent) of these patients, the rate of cure was appreciably below the 100 per cent for the cases in which the patients had not been previously treated (table 3).



The adverse effect of previous treatment on prognosis probably is largely due to the delay occasioned by the ineffective treatment. Some lesions remained healed superficially, and a long time elapsed before the remaining deep-lying cancer made itself evident.



Fig. 4.—*A*, basal cell carcinoma of group B (average diameter, 1 to 2 cm.), located in the nasofacial sulcus. It had repeatedly recurred after electrodesiccation, cauterization, roentgen ray and radium treatments over a period of five years. By the chemosurgical technic it was determined that the full thickness of the ala was cancerous, as was the periosteum of the maxillary bone of the cheek and lateral wall of the nasal cavity. *B*, healed lesion. The patient is free of cancer after four and one-half years.



Fig. 5.—*A*, basal cell carcinoma of group C (average diameter, 2 to 3 cm.). *B*, granulation tissue after the cancer had been removed in four microscopically controlled stages and after the final layer of fixed tissue had separated. *C*, healed lesion. The patient was free of cancer when he died, six years later.

*Effect of Histologic Grade of Malignancy on Prognosis.*—While there is no formal division of basal cell carcinomas into grades of malignancy, it is practical to designate them as either "invasive" or "non-

invasive." The invasive type is characterized by slender, poorly demarcated carcinoma cells with an indefinite basement membrane between them and the copious connective tissue stroma. The noninvasive type is composed of large, rounded clumps of basal cells, well demarcated by an intact basement membrane from the surrounding relatively meager stroma. Clinically, the invasive type is apt to show the erosion, ulceration and deep induration which is characteristic of the rodent ulcer (illustrated by figures 1, 3, 4, 5, 7, 8, 9 and 10), while the noninvasive type is apt to show the well defined, outgrowing lump characteristic of



Fig. 6.—*A*, basal cell carcinoma of group C. The lesion is of the nodular, outgrowing type, in contrast to the invasive lesions of the other patients herein pictured. *B*, granulation tissue after removal of final layer of fixed tissue. *C*, healed lesion. The patient is free of cancer after five years.

the nodular type of basal cell carcinoma (illustrated by figure 6). Intergradations between these two types are common.

In the 202 cases in the determinate group, 136 (67.3 per cent) were classified as invasive while the remaining 66 were called noninvasive.

TABLE 4.—*Effect of Histologic Grade of Malignancy of Basal Cell Carcinoma on Prognosis*

|                  | Number of Lesions | Successful Results |          |
|------------------|-------------------|--------------------|----------|
|                  |                   | Number             | Per Cent |
| Invasive.....    | 136               | 132                | 97       |
| Noninvasive..... | 66                | 66                 | 100      |

In the invasive group the rate of cure was 97 per cent, while in the noninvasive group successful results were obtained in 100 per cent (table 4).

Keratinization of some degree was observed in 21.3 per cent of the basal cell carcinomas in this series. In many cases there was sufficient keratinization to justify a diagnosis of basal-squamous cell carcinoma,

but separate classification was not deemed desirable, because these lesions behave the same as other basal cell carcinomas except that they are apt to be somewhat more invasive.

One pigmented basal cell carcinoma of the nose was treated by the chemosurgical technic, with a successful outcome.

*Effect of Site of Cancer on Prognosis.*—In the 202 cases of basal cell carcinoma in the determinate group, sixty-five lesions (32.2 per cent) started on the bridge of the nose, forty-eight (23.8 per cent) on



Fig. 7.—*A*, basal cell carcinoma, group C. It had recurred after sixteen roentgen ray and two radium treatments given over a three year period. *B*, granulation tissue, septal cartilage and nasal bone necessarily exposed due to the deeply invasive cancer. *C*, healed lesion. The small hole into the nasal cavity closed completely after two years. The patient is free of cancer after seven years.



Fig. 8.—*A*, basal cell carcinoma, group D (average diameter, over 3 cm.). *B*, lesion after separation of final layer of fixed tissue showing nasal bone, the periosteum of which had been cancerous, and the unsuspected extent of involvement at the periphery, especially in the right eyebrow. *C*, healed lesion. The patient is free of cancer after seven years.

the tip, forty-three (21.3 per cent) on the ala, twenty-five (12.4 per cent) on the root and twenty-one (10.3 per cent) in the nasofacial sulcus. None were encountered on the nasal septum.

Of the four lesions which failed to respond to chemosurgery, two started on the bridge, one on the tip and one in the nasofacial sulcus

(table 5). However, these lesions were so advanced that little or no nasal tissue remained, and the initial site was determined from the history. The most consistently difficult to eradicate were the lesions beginning in the nasofacial sulcus, because these lesions had a strong tendency to

TABLE 5.—*Effect of Site of Basal Cell Carcinomas on Prognosis*

| Site                   | Number of Lesions | Successful Results |          |
|------------------------|-------------------|--------------------|----------|
|                        |                   | Number             | Per Cent |
| Bridge.....            | 65                | 63                 | 96.9     |
| Tip.....               | 48                | 47                 | 97.9     |
| Ala.....               | 43                | 43                 | 100      |
| Root.....              | 25                | 25                 | 100      |
| Nasofacial sulcus..... | 21                | 20                 | 95.2     |
| Nasal septum.....      | ..                | ..                 | ...      |
| All sites.....         | 202               | 198                | 98       |

invade deeply in the embryologic fusion plane in this region. However, the microscopic control of excision afforded by the chemosurgical method made it possible to follow out and eradicate these deep extensions.

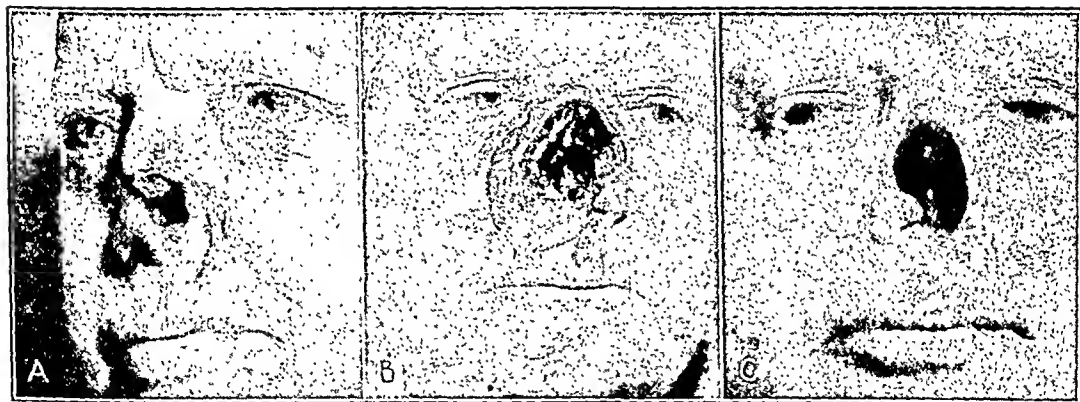


Fig. 9.—*A*, basal cell carcinoma, group D, which had started twenty-five years previously in the nasofacial sulcus and had recurred after application of solid carbon dioxide, electrodesiccation and twelve roentgen ray and six radium treatments. *B*, granulation tissue after the cancer had been removed in eight microscopically controlled stages and after most of the final layer of fixed tissue had separated, showing extensive involvement of nose, septum, maxillary bone and upper lip. *C*, healed lesion. The patient was fitted with a latex rubber prosthesis, and he remains free of cancer after four and one-half years.

#### THERAPEUTIC RESULTS IN CASES OF SQUAMOUS CELL CARCINOMA OF THE NOSE

Squamous cell carcinoma of the nose occurs much less frequently than the basal cell type. Thus, there were only thirty-three squamous cell carcinomas chemosurgically excised in the nine year period ending seven months prior to this writing.

*End Results After Six Months, Three Years and Five Years.*—The end results were calculated by the same means as were used in the section on basal cell carcinoma. In the six month period, successful results were obtained in 93.9 per cent of the 33 cases in the determinate group (table 6).

In the three year period, successful results were obtained in 87.5 per cent of 16 cases in the determinate group (table 6).

In the five year period, successful results were obtained in 81.8 per cent of 11 cases in the determinate group (table 6).

TABLE 6.—*End Results for Squamous Cell Carcinoma of the Nose After Periods of Six Months, Three Years and Five Years*

This series includes the cases of all patients with histologically proved squamous cell carcinoma, both early and advanced, previously untreated and recurrent, who were admitted to the chemosurgery clinic from July 20, 1926 to Oct. 21, 1941 for the six month group; from July 20, 1926 to July 17, 1942 for the three year group; from July 20, 1926 to July 3, 1940 for the five year group.

|   | Six<br>Month<br>Period | Three<br>Year<br>Period | Five<br>Year<br>Period |
|---|------------------------|-------------------------|------------------------|
| Total number of cases.....  | 33                     | 19                      | 12                     |
| Indeterminate group   |                        |                         |                        |
| Patients without recurrence dead from other causes.....   | 0                      | 3                       | 1                      |
| Patients without recurrence lost from observation.....  | 0                      | 0                       | 0                      |
| Total number .....  | 0                      | 3                       | 1                      |
| Determinate group   |                        |                         |                        |
| Total number .....  | 33                     | 16                      | 11                     |
| Unsuccessful results  |                        |                         |                        |
| Patients dead as a result of cancer.....  | 2                      | 2                       | 2                      |
| Patients with cancer lost from observation.....   | 0                      | 0                       | 0                      |
| Patients with cancer living.....  | 0                      | 0                       | 0                      |
| Total number .....  | 2                      | 2                       | 2                      |
| Successful results  |                        |                         |                        |
| Patients free from cancer for six months or more.....   | 31                     |                         |                        |
| Patients free from cancer for three years or more.....  | ..                     | 14                      |                        |
| Patients free from cancer for five years or more.....   | ..                     | ..                      | 9                      |
| Six month end results   |                        |                         |                        |
| Total number of cases with successful results divided by total number of determinate cases (31 ÷ 33)..... | 93.9%                  |                         |                        |
| Three year end results  |                        |                         |                        |
| Total number of cases with successful results divided by total number of determinate cases (14 ÷ 16)..... | ..                     | 87.5%                   |                        |
| Five year end results   |                        |                         |                        |
| Total number of cases with successful results divided by total number of determinate cases (9 ÷ 11).....  | ..                     | ..                      | 81.8%                  |

*Effect of Size of Lesion on Prognosis.*—The squamous cell carcinomas were divided into four groups, according to size: A, under 1 cm. in average diameter; B, 1 to 2 cm. (figs. 11 and 12); C, 2 to 3 cm., and D, over 3 cm.

There were only two unsuccessful results in the series: one in size group D and the other in group B (table 7). The former was in a patient with an extremely advanced carcinoma involving, besides the nose, the entire maxillary sinus and the orbit, with an extension of the carcinoma into the brain through the inferior orbital fissure, making it impractical to complete the removal of the neoplasm. The other unsuccessful result was in a patient with a septal lesion which proved to be much more advanced than the original measurement indicated. (Group-

ing as to size is made on the basis of the measurement taken before treatment is started, in order that the results of chemosurgical treatment may be compared with the results of other methods.) The patient was extremely uncooperative, and considerable difficulty was encountered in

TABLE 7.—*Effect of Size of Squamous Cell Carcinoma on Prognosis*

| Group           | Average Diameter, Cm. | Number of Lesions | Successful Results |          |
|-----------------|-----------------------|-------------------|--------------------|----------|
|                 |                       |                   | Number             | Per Cent |
| A.....          | Under 1               | 8                 | 8                  | 100      |
| B.....          | 1-2                   | 17                | 16                 | 94.1     |
| C.....          | 2-3                   | 4                 | 4                  | 100      |
| D.....          | 3 or more             | 4                 | 3                  | 75       |
| All groups..... |                       | 33                | 31                 | 93.9     |

keeping the dressings in place. The result was that the fixed tissues became dry and hard, which in turn made it difficult to obtain the usual thorough microscopic control. The patient was referred for roentgen therapy, but eventually metastases developed, causing the patient's death despite surgical dissection of the neck.

*Effect of Previous Treatment on Prognosis.*—In the 33 cases of squamous cell carcinoma in the determinate group, ten lesions (30.3 per



Fig. 10.—*A*, basal cell carcinoma, group D, which had started twenty-three years previously and had failed to heal after competent radium, surgical, radium seed and roentgen ray treatment over a period of twenty-one years. The patient had received no treatment during the last two years of this period because the prognosis was considered hopeless. *B*, lesion after excision of the cancer in twenty-five microscopically controlled stages and after the final layer of fixed tissue separated. Not only was the entire nose cancerous but also involved were the septum (except for the strip in front of the applicator), the turbinates, all the walls of the nasal cavity, the left antrum, the mucosal portion of the upper lip, the anterior half of the hard palate, the periosteum of the right cheek bone and the floor of the right orbit. The orbital portion extended posteriorly to the orbital rim for 2 cm. (where applicator is inserted), but the eyeball was uninvolved, so the vision of this one remaining eye was preserved. *C*, healed lesion (except for the right cheek, from which a piece of necrotic bone had just been removed). The patient is free of cancer after nearly four years and is now undergoing plastic repair.

cent) had recurred after previous unsuccessful treatment by surgical or radiation therapy. Of the 10 patients it was possible to salvage 9 (90 per cent), while of the group of 23 patients whose lesions had not been previously treated 22 (95.6 per cent) were salvaged (table 8).

*Effect of Histologic Grade of Malignancy on Prognosis.*—Classification of the thirty-three squamous cell cancers of the nose on the basis of Broder's four grades of malignancy revealed a strong correlation

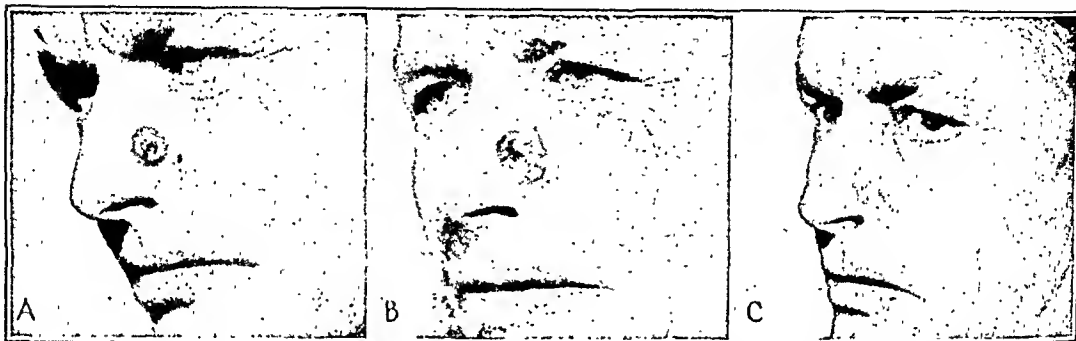


Fig. 11.—*A*, squamous cell carcinoma, group B (average diameter, 1 to 2 cm.). It grew rapidly since its onset two months previously. *B*, granulation tissues after removal of the squamous cell carcinoma in six microscopically controlled stages and after separation of the final layer of fixed tissue. The carcinoma, which was of grade 3 malignancy, extended to within 2 mm. of the nasal mucosa. *C*, healed lesion. There is no evidence of cancer after fourteen months.

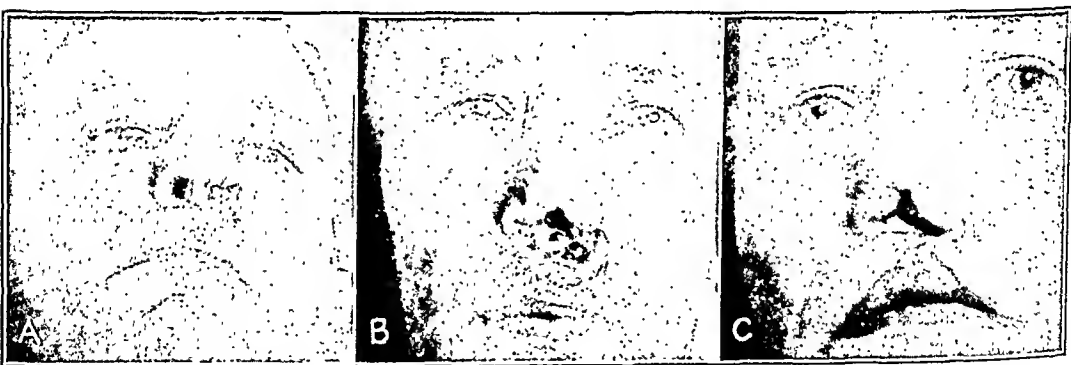


Fig. 12.—*A*, squamous cell carcinoma, group B, involving the nasal septum. It had recurred after repeated electrodesiccation and cauterization treatments over a period of three years. *B*, lesion after excision of the cancer in thirteen microscopically controlled stages. The neoplasm had eroded through the upper lip into the gingivolabial sulcus and had involved a large portion of the nasal septum. *C*, healed lesion. The patient is free of cancer after four and one-half years.

between histologic structure and prognosis (table 9). While successful results were obtained in all cases in the grade 1 and grade 2 groups, only 4 of 6 patients in the grade 3 group were successfully treated. There were no cases in the grade 4 group.

*Effect of Site of Cancer on Prognosis.*—In the 33 cases of squamous cell carcinoma of the nose in the six month period, twelve (36.4 per cent) of the lesions started on the bridge, eight (24.2 per cent) on the ala, five (15.2 per cent) on the tip, six (18.2 per cent) on the septum and two (6 per cent) on the root. None started in the nasofacial sulcus (table 10).

Lesions in all these sites were successfully treated, with the exception of the carcinoma on the ala and the carcinoma on the septum, which lesions were described in the section on the effect of size on prognosis.

TABLE 8.—*Effect of Previous Unsuccessful Treatment of Squamous Cell Carcinoma on Prognosis*

|                           | Number of Patients | Successful Results |          |
|---------------------------|--------------------|--------------------|----------|
|                           |                    | Number             | Per Cent |
| Previously treated.....   | 10                 | 9                  | 90       |
| Previously untreated..... | 23                 | 22                 | 95.6     |

TABLE 9.—*Effect of Histologic Grade of Malignancy of Squamous Cell Carcinoma on Prognosis*

| Grade  | Number of Lesions | Successful Results |          |
|--------|-------------------|--------------------|----------|
|        |                   | Number             | Per Cent |
| 1..... | 10                | 10                 | 100      |
| 2..... | 17                | 17                 | 100      |
| 3..... | 6                 | 4                  | 66.6     |
| 4..... | ..                | ..                 | ...      |

TABLE 10.—*Effect of Site of Squamous Cell Carcinoma on Prognosis*

| Site                   | Number of Lesions | Successful Results |          |
|------------------------|-------------------|--------------------|----------|
|                        |                   | Number             | Per Cent |
| Bridge.....            | 12                | 12                 | 100      |
| Tip.....               | 5                 | 5                  | 100      |
| Ala.....               | 8                 | 7                  | 87.5     |
| Root.....              | 2                 | 2                  | 100      |
| Nasofacial sulcus..... | ..                | ..                 | ...      |
| Nasal septum.....      | 6                 | 5                  | 83.3     |
| All sites.....         | 33                | 31                 | 93.9     |

*Effect of Metastasis on Prognosis.*—In only 2 cases of this series did metastases develop. In 1 case the metastasis, which was secondary to a carcinoma replacing the entire nose, was an outlying nodule in a lymphatic vessel near the inner canthus; both primary and secondary lesions were chemosurgically excised, with a successful outcome. The other case was one of unsuccessfully treated carcinoma of the septum previously mentioned; the patient died of metastases after an unsuccessful



ful surgical dissection of the neck. In the first case the carcinoma was large and pendulant, while in the second there was invasion into the upper lip; it is suggested that the movement of the neoplasms as a consequence of these factors may have squeezed cancer cells out into the lymphatics. However, since most cancers of the nose are not subject to motion, metastasis is infrequent in this site.

#### THERAPEUTIC RESULTS FOR OTHER NEOPLASMS OF THE NOSE

The microscopic control of excision afforded by the chemosurgical method is also advantageous in the treatment of other neoplasms of the nose.

*Hemangioma.*—One hemangioma in the nasopharynx was successfully removed by a modified chemosurgical technic after surgical and radium treatment had failed, mainly due to profuse hemorrhage. The mass, which was 3 cm. in diameter, was attached to the posterior wall of the nasopharynx. It was treated by the application of small squares of gauze which had been impregnated with the zinc chloride fixative. Since the mass was too far back to admit a scalpel, the fixed tissue was allowed to slough, after which the fixative was reapplied. By treatment of it every third day, the mass was eradicated without hemorrhage. The patient remains well after eight years.

*Nevus.*—Five nevi, both with and without pigment, were chemosurgically removed from the nose. None are known to have recurred, and in none has melanomatous change occurred after periods of observation of from one month to eight years. Complete removal was assured by the microscopic sections made to determine the depth of the lesion.

*Adenoma.*—Two sebaceous adenomas and one sweat gland adenoma were chemosurgically removed, with no return after periods of from one to eight years.

*Cyst.*—Two sebaceous cysts and two epidermoid cysts were successfully removed by chemosurgical measures. Cysts may be treated by cauterizing the central portion with dichloroacetic acid and, after a few minutes, opening the lesion, draining the contents and cauterizing the lining. Microscopic control in the treatment of these lesions is usually not necessary.

#### THERAPEUTIC RESULTS IN PRECANCEROUS LESIONS OF THE NOSE

*Senile Keratosis.*—The treatment of senile keratoses depends on the clinical appearance of the lesions. If the lesion is clearly inactive, it is sufficient to pull or scrape off the horny portion of the lesion and then thoroughly cauterize the base with dichloroacetic acid. However, if the lesion is raised, indurated or ulcerated, it is much safer to excise

the lesion chemosurgically and examine it microscopically so that no deep downgrowths of precancerous epithelium are left behind. No instance of recurrence or malignant change is known to have occurred after periods up to nine years in any of thirty-five senile keratoses of the nose treated in this way.

*Chronic Ulceration.*—There were 2 instances of chronic ulceration, with peripheral epithelial hyperplasia, located on the septum or the floor of the nose. The ulcerations were chemosurgically excised, and healing was uneventful and permanent.

#### COMMENT

In common with many cancers in accessible sites, cancer of the nose is often characterized by considerable irregularity of shape. That is, in addition to the grossly visible main tumor mass there are often irregular outgrowths of cancer in tissues with reduced resistance to cancer spread, such as periosteum, perichondrium, perineurium, lymphatics and embryologic fusion planes. Most of these outgrowths are not initially demonstrable, even by careful clinical examination, and it is only by the systematic microscopic control attained with the chemosurgical technic that each of these extensions can be accurately followed out and eradicated. This accurate control of excision results not only in unprecedented reliability but also in maximum sparing of uninvolved tissues.

The results here presented adequately indicate the great reliability of the chemosurgical method in the treatment of carcinoma of the nose. For basal cell carcinoma the rates of cure were 98 per cent at six months, 97.2 per cent at three years and 94.3 per cent at five years. For squamous cell carcinoma the rates of cure were 93.9 per cent at six months, 87.5 per cent at three years and 81.8 per cent at five years. These records were attained in spite of the fact that many of the lesions were far advanced and over a third were recurrent after previous unsuccessful irradiation or surgical treatment.

The results obtained by the chemosurgical treatment of carcinoma of the nose compare favorably with those obtained by other methods. One of the few series large enough to use for comparison is that of Magnusson,<sup>5</sup> who reported on the results obtained with the highly developed radiologic, surgical and electrosurgical technics employed at the *Radiumhemmet* in Stockholm. From his protocols it was determined that his three year rate of cure for basal and squamous cell carcinoma of the nose was 92.7 per cent. In the present series the rate of cure obtained by chemosurgery was 96 per cent; this record was attained

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5. Magnusson, A. H. W.: Skin Cancer: A Clinical Study with Special Reference to Radium Treatment, *Acta radiol.* 1935, supp. 22, pp. 1-287.

despite the fact that a higher proportion of my cases were in the groups of the larger-sized lesions (30.4 per cent were in the size groups C and D, as compared with 18.7 per cent in Magnusson's series) and despite the fact that more of my patients had been previously unsuccessfully treated (40.8 per cent in the three year period as compared with 28 per cent in Magnusson's series).

The reliability of the chemosurgical method is not attained by an excessively radical approach. Quite the opposite, not more than 1 or 2 mm. of tissue beyond the actual extent of carcinomatous invasion is destroyed.

The lack of operative risk is a further advantage. In this series, no deaths resulted from chemosurgical treatment, although many of the patients were old and in poor health.

Though the technic entails a considerable amount of hard, tedious work for the far advanced cancers, the great majority of lesions do not require an undue expenditure of time and effort.

#### SUMMARY AND CONCLUSIONS

The chemosurgical treatment of cancer of the nose has the great advantage of thorough microscopic control of excision. This control is responsible for the unprecedented reliability and the conservatism of the method.

The reliability of the method is indicated by the unusually high proportion of successful results. Thus, for basal cell carcinoma, successful results were obtained in 98 per cent of 202 cases observed for six months or more, in 97.2 per cent of 109 cases in the three year period and in 94.3 per cent of 53 cases in the five year period. For squamous cell carcinoma the rate of cure was 93.9 per cent for the 33 cases in the six month period, 87.5 per cent for the 16 cases in the three year period and 81.8 per cent for the 11 cases in the five year period. These results were obtained despite the fact that many of the cancers were far advanced and over one third had recurred after previous irradiation or surgical treatment.

The method is conservative, since only 1 or 2 mm. of tissue are removed beyond the points of actual carcinomatous invasion.

The method is also useful in the treatment of various benign neoplasms and of precancerous lesions of the nose.

## NEW METHOD OF LEG EXERCISES

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THE DRAMATIC episode of pulmonary embolism is shocking to the surgeon who suddenly loses his patient in the wake of an apparently uneventful recovery. It is not surprising, therefore, that this tragic event, although of no great frequency, became the topic of numerous investigations dealing with its causes, prevention and treatment.

Three distinct groups of factors can be distinguished in the causation of phlebothrombosis and the resulting embolism: (1) retardation of the venous flow, (2) structural changes in the wall of the affected blood vessels, especially in the endothelium, and (3) changes in the constituents of the blood and chemical changes responsible for coagulation of the blood.

The majority of authors agree that the first-mentioned factor, namely, the retardation of the venous flow, for which lack of muscular contractions is chiefly responsible, is of paramount importance in the genesis of thrombus with resulting embolism. It follows that stimulation of vascular flow should go a long way in the prevention of postoperative pulmonary embolism. In view of the fact that the commonest source of thrombosis leading to embolism is the femoral vein and its tributaries,<sup>1</sup> the lower extremities are receiving the greatest attention in attempts to prevent slowing of the blood stream and associated vascular clotting. Pool<sup>2</sup> suggested a set of active exercises and early ambulation. Various devices have been developed for the same purpose; rollers, against which the patient is instructed to rub his feet and legs<sup>3</sup>; rhythmically contracting air cushions strapped to the patient's legs<sup>4</sup>; levers raising and lowering the patient's limbs<sup>4</sup>;

1. Henderson, E. F.: Fatal Pulmonary Embolism, *Arch. Surg.* **15**:231 (Aug.) 1927. Graves, W. N.: *Surg., Gynec. & Obst.* **70**:958, 1940.

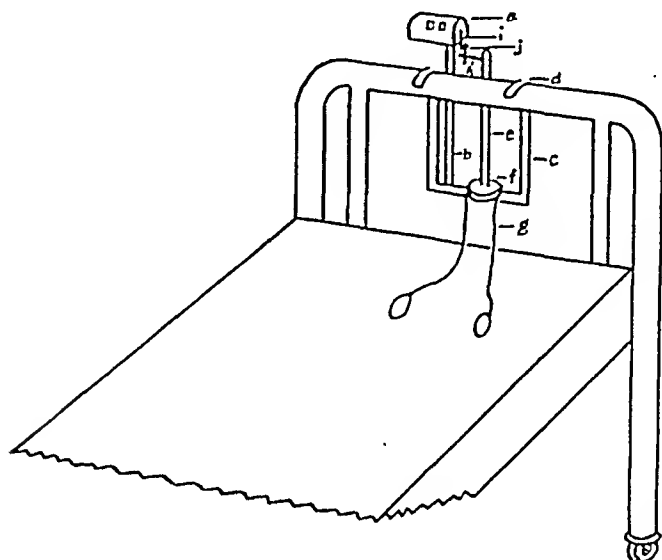
2. Pool, E. H.: Systematic Exercises in Postoperative Treatment, *J. A. M. A.* **60**:1202 (April 19) 1913.

3. Shaw, W. F., and Rickards, C. E. B.: *J. Obst. & Gynaec. Brit. Emp.* **45**:451, 1938.

4. Robertson, H.: *Am. J. Surg.* **41**:3, 1938.

pedaling apparatus,<sup>5</sup> and a device consisting of a stand which carries two pulleys with counterbalance weights.<sup>6</sup>

The efficiency of postoperative exercises in prevention of pulmonary embolism is attested by Erskine and Shires,<sup>7</sup> who reported that the incidence of fatal embolism after abdominal operations was reduced by more than half following the introduction of postoperative exercises



Leg exerciser.

and massage. Fletcher Shaw and Rickards<sup>3</sup> found fatal embolism to be five times commoner in a hospital where exercises are not included in the postoperative treatment as compared with another institution where exercises are carried out as a routine.

On the other hand, certain disadvantages of the aforementioned devices should be mentioned: Most of them are bulky and cumbersome; either they take considerable space in the bed, affecting the patient's comfort, or they protrude from the bed, interfering with a free passage in the room; patients must be uncovered to perform the exercises; some devices are impractical or expensive; they are time consuming because they require supervision, and, finally, they provide no facilities for registration, which is essential because pain or lack of interest caused by sedation may prevent the patient from faithfully exercising his legs.

5. Gamble, H. A.: *Am. J. Surg.* **28**:93, 1935. Cogswell, H. D., and Thomas, C. A.: *Surgery* **10**:323, 1941.

6. Gambill, I. M., and Kamenshine, A.: *M. Bull. Vet. Admin.* **20**:173, 1943.

7. Erskine, J. P., and Shires, I. C.: *J. Obst. & Gynaec. Brit. Emp.* **52**:480, 1945.

To overcome such drawbacks, the authors developed an apparatus which is inexpensive, simple in construction, takes practically no space, allows the patient to remain covered and permits registration of the movements of the legs. Such a device saves valuable time of the understaffed nursing personnel, induces the patient to carry out the instructions and offers an easy way for a check-up. The exercises can be graded, increasing in number with the progress in the patient's condition.

#### DESCRIPTION OF THE APPARATUS

The apparatus consists essentially of a counting machine (*a*) mounted on a bracket (*b*) of an aluminum U-frame (*c*) whose both ends are hook shaped (*d*) so that they can be hung over the foot of the bed. A vertical shaft (*e*) which rises from the center of the transverse portion of the frame supports a pulley (*f*). Both looped ends of a sash cord (*g*) which rides around the pulley are attached to the patient's feet. A horizontal rod (*h*) attached to the top end of the vertical shaft trips the arm lever (*i*) of the counter whenever the pulley rotates. The lever is equipped with a hinged end piece (*j*), which permits tripping of the lever only in one direction.

#### SUMMARY

A new device for exercising the legs is described, which offers the following advantages in comparison with similar devices: 1. It has a simple construction and can be attached to the foot of the bed without any screws or clamps. 2. It is compact. 3. It can be used without uncovering the patient. 4. It is inexpensive. 5. It is provided with a counting machine, which permits graded exercises without supervision by the nursing personnel.

1200 North Ashland Avenue.

## REACTION OF TISSUE TO AND THE FATE OF OXIDIZED CELLULOSE IN THE PERITONEAL CAVITY OF THE DOG

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FOREIGN substances which can be left in tissues have been used for some time in various fields of surgery. Relatively nonirritating materials, such as metal plates, screws and wire, have been used in the open reduction of fractures, but these rarely cause trouble unless infection is present.

Silk, cotton and nylon used for ligature are usually introduced in such small amounts that they become clothed in varying amounts of fibrous tissue and lead to no further trouble. Surgical gut, though more irritating to the tissues, is completely absorbed. Large amounts of gauze, usually in the form of sponges, accidentally left in the tissues usually result in some complicating reaction sooner or later.

Gauze packs are used sometimes to promote adhesions and, when they have accomplished this purpose, are removed with impunity. However, there are occasions when such packs are used for purposes of hemostasis, but their removal may initiate fresh bleeding. Then, too, infection may easily be introduced in such a wound, and a gauze pack not only inhibits drainage but may obscure such infection.

Therefore, a gauzelike material which can be left in tissues and which causes no untoward reaction therein is highly desirable.

Cellulose is the term applied to a class of compounds which, in common with starch and glycogen, may be designated by the empiric formula  $(C_6H_{10}O_5)_x$  and classified as hexosans or glucosans. On complete hydrolysis, cellulose from any source yields glucose. Cellulose occurs in the fibrous or supporting tissues of plants and in the walls of plant cells. It occurs in relatively pure form in cotton.<sup>1</sup>

Oxidized, or absorbable, cellulose has been prepared by Kenyon<sup>2</sup> and associates. The cellulose was oxidized by the action of nitrogen

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From the Department of Surgery, St. Louis University School of Medicine.

The material with which this work was done was supplied by Parke, Davis & Company, Detroit.

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2. (a) Unruh, C. O., and Kenyon, W. O.: *Investigation of the Properties of Cellulose Oxidized by Nitrogen Dioxide*, J. Am. Chem. Soc. **64**:127, 1942. (b) Yackel, E. C., and Kenyon, W. O.: *The Oxidation of Cellulose by Nitrogen Dioxide*, J. Am. Chem. Soc. **64**:121, 1942.

dioxide on it in a closed chamber. The cellulose was then air dried after having been washed with distilled water. There was no shrinkage in amount. Depending on the amount of oxidation, oxidized cellulose with various contents of carboxyl (COOH) groups are obtained. Oxidized celluloses, having contents of carboxyl groups up to 15 per cent are fluffy white materials, which cannot be distinguished from the original cellulose by visual examination and are not friable and the fibers of which do not break up when handled. Materials having carboxyl contents greater than 15 per cent maintain their fibrous structure, but there is some shrinkage, accompanied with surface hardening.

Alkali solubility (usually 10 per cent sodium hydroxide) is employed as a test of the oxidation of cellulose. The products of mild oxidation are usually only partially soluble, while those of vigorous oxidation dissolve completely. Celluloses whose content of carboxyl groups is above 13 per cent dissolve in dilute aqueous solutions of inorganic or organic bases, while celluloses with less than 13 per cent content of carboxyl groups do not dissolve.

Seegers and Doub<sup>3</sup> found that oxidized cellulose contains approximately 20 per cent of carboxyl groups.

Oxidized cellulose in the form of gauze is sterilized with solution of formaldehyde, which does not leave a trace of formaldehyde sufficient to render the material irritating. It is then doubly packaged in individual sterile envelopes. It cannot be reautoclaved, since it disintegrates, but may be boiled three minutes or kept in 70 per cent alcohol until used.<sup>4</sup>

The gauze is 3 inches (7.5 cm.) square, and the thickness is 8 ply. It is white, with a slight yellow tinge, and is somewhat more friable than ordinary gauze.

Heidelberger and Hobby<sup>5</sup> have shown that oxidized cellulose contains an immunologically specific polysaccharide.

Experiments were carried out in which oxidized cellulose was placed in the peritoneal cavities of dogs and the effect observed.

The animals used were ordinary mongrel dogs of various sizes and weights and of both sexes. Intravenous injections of pentobarbital sodium were used for anesthesia, and the operation was done under sterile conditions, a right rectus incision being used. In every case the peritoneal cavity was uninfected.

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3. Seegers, W. H., and Doub, L.: Oxidized Cellulose and Thrombin, *Proc. Soc. Exper. Biol. & Med.* **56**:72, 1944.

4. Uihlein, A.; Clagett, O. T.; Osterberg, A. E., and Bennett, W. A.: Absorbable Oxidized Cellulose with Thrombin as a Hemostatic Agent in Surgical Procedures, *Surg., Gynec. & Obst.* **80**:470, 1945.

5. Heidelberger, M., and Hobby, G.: Oxidized Cotton: An Immunologically Specific Polysaccharide, *Proc. Nat. Acad. Sc.* **28**:516, 1942.



TABLE 1.—*Oxidized Gauze 2 x 1 cm. (8 Ply)*

| Dog | Time,<br>Days | Gross Appearance of Gauze      |                     |                    |   | Microscope Appearance of Gauze   |
|-----|---------------|--------------------------------|---------------------|--------------------|---|--|
|     |               | Between Liver<br>and Diaphragm | Among<br>Intestines | In Pelvis          | In Omental Bursa  |  |
| 1   | 1             | Small brown<br>mass            | Gelatinous<br>mass  | Gelatinous<br>mass | Brown gelatinous mass   | There is a moderate inflammatory reaction, characterized by neutrophilic infiltration and congestion of blood vessels; surrounding tissue intensely inflamed   |
| 2   | 2             | Brownish<br>gelatinous<br>mass | Brownish<br>spot    | Absorbed           | Dark brownish gelatinous<br>mass                                    | There is a more pronounced neutrophilic infiltration of the gauze; otherwise the reaction is the same as that seen in the above section  |
| 3   | 3             | Absorbed                       | Absorbed            | Absorbed           | Scumlike, brownish<br>gelatinous mass                               | The inflammatory reaction is less intense, but in addition to the neutrophilic infiltration of the fibers, there are many macrophages present; these are relatively large and round, with clear, slightly basophilic cytoplasm |
| 4   | 4             | Absorbed                       | Absorbed            | Absorbed           | Approximately one-half<br>original size; gelati-<br>nous; semisolid | There is beginning disintegration of the gauze fibers, and fibroblasts are seen in the inflammatory exudate surrounding the gauze and its individual fibers  |
| 11  | 8             | Absorbed                       | Absorbed            | Absorbed           | No evidence of gauze<br>found                                       | No section made  |
| 13  | 11            | Absorbed                       | Absorbed            | Absorbed           | Approximately one-half<br>original size; brownish<br>fibers         | There is still an intense inflammatory reaction in the tissue surrounding the gauze; the gauze is infiltrated by large numbers of the macrophages mentioned, with a more complete disintegration of the gauze                  |
| 8   | 17            | Absorbed                       | Absorbed            | Absorbed           | Few dark brownish fibers  | Few gauze fibers are seen; many macrophages are still present, but in addition many more fibroblasts are seen  |
| 5   | 21            | Absorbed                       | Absorbed            | Absorbed           | Small brownish spot   | Only a few gauze fibers are seen; these are almost completely disintegrated and are surrounded by large numbers of macrophages, whose cytoplasm is filled with dark granular brownish-staining materials                       |
| 7   | 23            | Absorbed                       | Absorbed            | Absorbed           | Small brownish spot   | No section made  |
| 9   | 23            | Absorbed                       | Absorbed            | Absorbed           | Small brownish spot   | No section made  |
| 10  | 23            | Brown spot                     | Absorbed            | Absorbed           | Tannish stain   | One small gauze fiber is seen, surrounded by macrophages, fibroblasts, fibrocytes and a few neutrophils  |

In the first group of animals, pieces of cellulose in the form of gauze were placed in various positions in the peritoneal cavities. The gauze measured 2 by 1 cm., and the thickness was 8 ply. Such pieces of gauze were placed as follows: (*a*) in the omental bursa, (*b*) between the right side of the diaphragm and the liver, (*c*) among the intestines, (*d*) in the pelvis. Only gauze was introduced into the peritoneal cavity, as it was not desired that sutures to hold the gauze in place or for purposes of marking should be present possibly to influence the reaction.

The peritoneal cavities of the animals were reopened, each at a different time, until such time as the gauze was absorbed, and sections from omental bursa were taken for microscopic study.

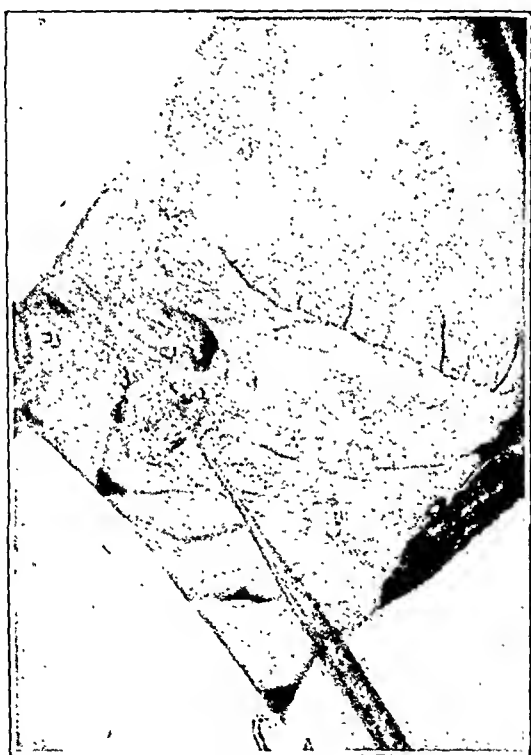


Fig. 1.—Appearance of the gauze in the omental bursa after three days.

Table 1 summarizes the results obtained with this group.

Macroscopically, the gauze forms a gelatinous brownish mass, which primarily is larger than the original mass of the gauze but gradually decreases in size as it is completely absorbed. Figure 1 illustrates the appearance of the gauze placed in the omental bursa after three days.

Microscopically, there is in the early stages a moderate acute inflammatory reaction, with many neutrophils present. Fibroblasts are seen

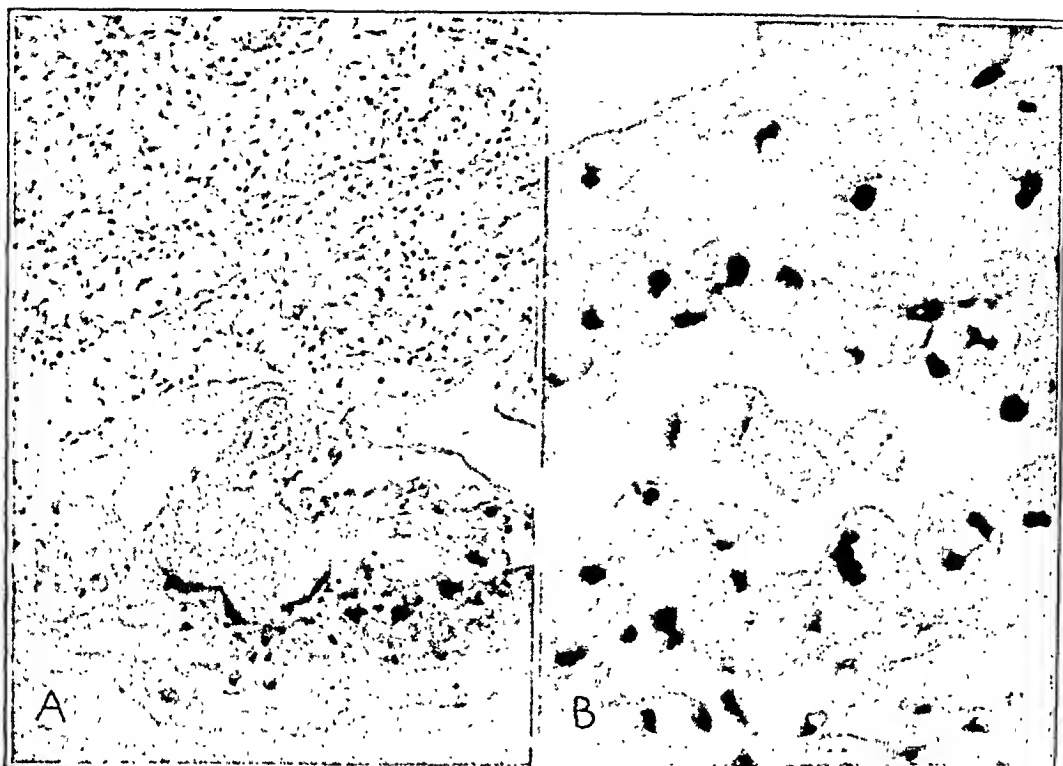


Fig. 2.—Large rounded macrophages with basophilic-staining granules in the cytoplasm after eleven days. *A*,  $\times 10$ ; *B*,  $\times 44$ .

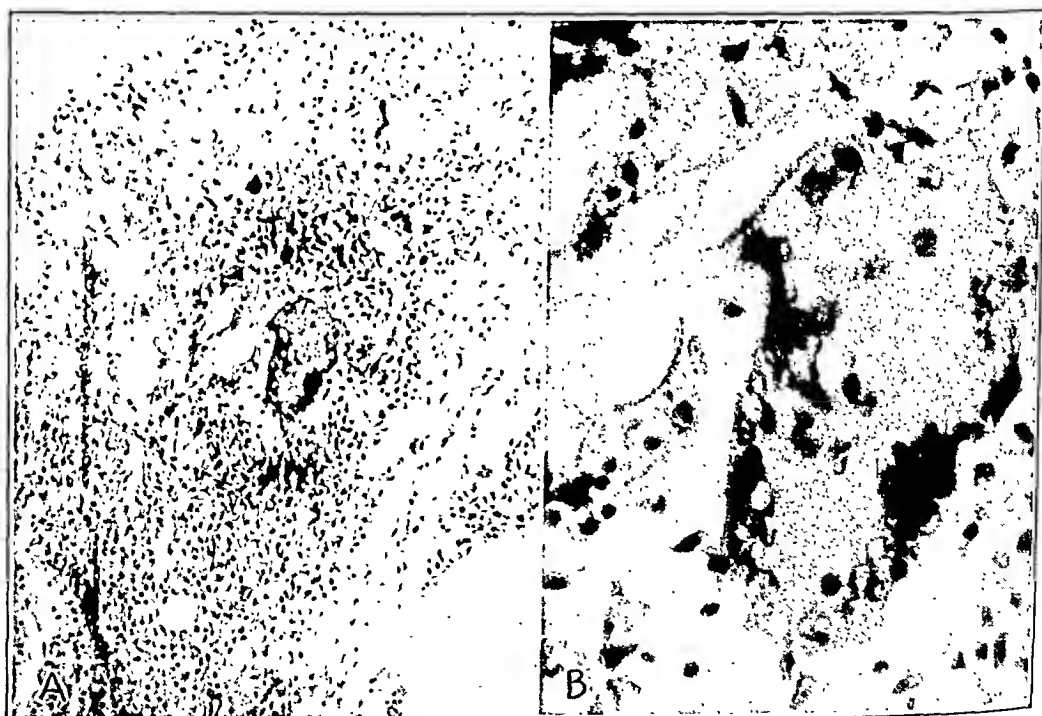


Fig. 3.—*A*, moderate number of macrophages and neutrophils are present, surrounding the one gauze fiber seen in the center of the photograph. There are also numerous fibroblasts ( $\times 10$ ). *B*, infiltration of the fiber by the cellular exudate ( $\times 44$ ).

in the inflammatory exudate on the fourth day, and on the eleventh day large numbers of macrophages are seen around the gauze. The latter cause a further disintegration of the gauze, the fibers gradually decreasing in size until complete disappearance.

The photomicrographs illustrate some of the features mentioned.

Figure 2 (*A*,  $\times 10$  and *B*,  $\times 44$ ) shows the presence of large numbers of large rounded macrophages, with slightly basophilic-staining granules in the cytoplasm after eleven days.

Figure 3 (*A*,  $\times 10$  and *B*,  $\times 44$ ) shows the appearance of the gauze after seventeen days. One gauze fiber is seen in the center of the photograph. A moderate number of macrophages and neutrophils are present surrounding the gauze, but in addition there are numerous fibroblasts. Figure 3 *B* demonstrates infiltration of the fiber by the cellular exudate.

TABLE 2.—*Oxidized Gauze 4 x 2 cm. (8 Ply)*

| Dog | Time, Days | Gross Appearance of Gauze  |
|-----|------------|--|
| 14  | 10         | Tiny brownish spot found on serosal surface of small intestine                                     |
| 16  | 10         | One small brownish fiber found adherent to serosal surface of small intestine; no adhesions formed |
| 18  | 10         | No trace of any gauze found; no adhesions formed   |

TABLE 3.—*Oxidized Gauze 4 x 4 cm. (8 Ply)*

| Dog | Time, Days | Gross Appearance of Gauze   |
|-----|------------|---|
| 15  | 14         | Small brownish fiber found approximately 4 x 1 mm., adherent to mesentery of small intestine; no adhesions formed |
| 17  | 13         | No gauze found; no adhesions formed   |
| 19  | 14         | No gauze found; no adhesions formed   |

In the second and third groups (tables 2 and 3 respectively), the gauze was placed between loops of small intestine.

### CONCLUSIONS

Oxidized gauze is completely absorbed in the peritoneal cavity of the dog. A brownish gelatinous mass is formed, which gradually decreases in size until it is finally absorbed.

A piece of oxidized gauze 2 by 1 cm. (8 ply) is completely absorbed in the omental bursa of the dog in approximately twenty-eight days. A piece of the size described when placed among the intestines is completely absorbed in two days. A piece of oxidized gauze 4 x 2 cm. (8 ply) when placed among the intestines is completely absorbed in approximately ten days, while a piece 4 by 4 cm. (8 ply) similarly placed is completely absorbed in approximately thirteen days.

In some cases, during the process of absorption fibrinous adhesions are formed, but after complete absorption no adhesions are formed and there is no visible trace of the gauze.

Systemic changes, i. e., fever, leukocytosis, increase in pulse rate and increase in sedimentation rate, were not recorded, because there was no adverse systemic clinical condition observed.

The absorption of the gauze may, in part at least, be due to solution by the tissue juices,<sup>6</sup> but a large part of the absorption is definitely due to digestion by macrophages.<sup>7</sup>

The variability of the time for absorption may be due to the amount of the gauze present, the degree of oxidation of the gauze (products with less than about 13 per cent of carboxyl groups do not dissolve),<sup>2b</sup> uniformity of the oxidation of the gauze, the nature of the tissue, the amount and type of peritoneal fluid present and the mechanical motility of the surrounding tissues (in this case, abdominal viscera).

It occurred to me that oxidized cellulose might well be used as an effective substitute when the use of a gauze pack is deemed necessary. It may also be used for hemostasis,<sup>8</sup> either by itself or in combination with some blood derivatives such as thrombin, but I made no effort to verify these suppositions by tests, because they were not within the province of this thesis.

#### SUMMARY

1. Oxidized cellulose forms a brownish gelatinous mass, which gradually decreases in size until it is completely absorbed in the peritoneal cavity of the dog.

2. The rate of absorption depends on the amount of gauze (cellulose) present.

3. No intraperitoneal adhesions are formed after complete absorption of the gauze.

4. The absorption is due in a large part to phagocytosis.

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6. Frantz, V. K.: Absorbable Cotton, Paper and Gauze (Oxidized Cellulose), *Ann. Surg.* **118**:116, 1943.

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## NONTRAUMATIC SPONTANEOUS RUPTURE OF THE SPLEEN

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**N**ONTRAUMATIC spontaneous rupture of an apparently normal spleen, considered by some as an impossibility, is indeed a rarity. Ask-Upmark<sup>1</sup> studied a total of 120 cases of rupture of the spleen, and it included only 2 cases in which the history was absolutely negative regarding trauma. One of the cases concerned a 43 year old man in whom the ruptured spleen was macroscopically normal. No microscopic examination was made. The other case was that of a 30 year old man. The ruptured spleen weighed 250 Gm., and it contained no coagula. The microscopic examination showed hyalinization of the arterioles and increase of stroma. Ask-Upmark concluded that a spontaneous rupture of a normal spleen is possible, explaining it on a basis of a functional lienal apoplexy.

Zuckerman and Jacobi<sup>2</sup> reported a case of genuine spontaneous rupture of a normal spleen in a 29 year old woman, with a report of the autopsy. Reviewing some 28 cases, 21 genuine and 7 dubious, they concluded that there exist cases of genuine nontraumatic spontaneous splenic rupture. In their case, the spleen, removed at autopsy, measured 17 by 9.5 by 5 cm. and weighed 385 Gm. Microscopic examination of the spleen showed all the sinuses extremely distended, with masses of well preserved erythrocytes in large numbers. No other changes were noted. Microscopic examination of the other organs showed only severe anemia.

Dahle<sup>3</sup> found 14 cases in the literature in which trauma could positively be excluded; yet rupture of entirely normal spleens occurred.

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1. Ask-Upmark, E.: On the Question of the Pathogenesis of So-Called Spontaneous Ruptures of the Spleen, with Some Remarks on the Symptomatology, *Klin. Wchnschr.* 16:897 (June 19) 1937.

2. Zuckerman, I. C., and Jacobi, M.: Spontaneous Rupture of the Normal Spleen, *Arch. Surg.* 34:917 (May) 1937.

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His case was that of an 18 year old boy, and the surgically removed spleen, with recovery of the patient, was normal macroscopically and microscopically.

Shafir,<sup>4</sup> reviewing the literature, found 34 cases and added 1 of his own. He concluded that rupture of the macroscopically and microscopically normal spleen is a rarity but does occur. Müller<sup>5</sup> reported 1 case and concluded similarly.

On the other hand, Lundell<sup>6</sup> found 20 cases in the literature which were designated as spontaneous rupture of a healthy spleen either by the authors themselves or by other authors. Subjecting these to a critical evaluation, Lundell did not find a single case in which it was clearly demonstrated that a healthy spleen may rupture spontaneously.

Rubnitz<sup>7</sup> stated that "A normal spleen will not rupture unless it is subjected to violence of a considerable degree. Rupture of the spleen in the absence of obvious trauma is an indication that deep-seated degenerative and necrotic changes have taken place."

#### REPORT OF A CASE

*History.*—W. W., a white man aged 46, an inspector of rubber goods, was seen by one of us (I. S.) on Sunday April 8, 1945, about 4 p. m., while he was in a state of semishock. The history given was that the patient had enjoyed normal good health up to a few hours before. He had been working regularly an eight hour day shift six days a week until Saturday, April 7, at 3 p. m. On Sunday, between 8 and 10 a. m., he partook of ham, eggs, coffee and similar food. At 12 noon he ate his usual Sunday dinner. At 1:30 p. m., while out in the back yard relaxing, he was seized suddenly with violent and excruciating pain in the lower part of the abdomen. Usual household remedies such as enema, ice bag and sodium bicarbonate failed to give relief. His condition became worse.

The patient was absolutely certain that he had not injured any part of his body. He never had any symptom referable to the gastrointestinal system, he never suffered from malaria or typhoid fever and he had never been out of the state of New Jersey, his birthplace. He had had lobar pneumonia in 1925. There had been no recent loss of weight. The patient drank an occasional glass of beer and smoked moderately. He had enjoyed normal health for the past twenty years, up to his recent illness. These facts were obtained time and again, with no variation.

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4. Shafir, L.: Spontaneous Rupture of Normal Spleen, *Vestnik khir.* **60**:574, 1940.

5. Müller, J. X.: Spontaneous Hemorrhages of the Spleen, *Chirurg* **12**:265 (May 1) 1940.

6. Lundell, G.: Spontaneous Rupture of the Spleen, *Acta chir. Scandinav.* **75**:547, 1934.

7. Rubnitz, A. S.: Spontaneous Rupture of the Spleen Due to Acute Leukemia or Acute Leukemia Due to Trauma to Spleen—Which? *J. Lab. & Clin. Med.* **28**:972 (May) 1943.

*Physical Examination.*—The patient was restless, tossing from side to side, with beads of cold, clammy perspiration on his drawn pale face. His lips were dry. The pulse rate was 120 and the respiratory rate 24 per minute. His temperature was 98.0 (37.7 C.) per mouth. The examination of the chest exhibited no pathologic changes. The abdomen, somewhat distended, was difficult to palpate because the patient assumed a voluntary rigidity of the abdominal muscles and with his hands warded off the examiner's palpating hand. A diagnosis of a ruptured abdominal organ was made and immediate hospitalization insisted on.

*Course and Treatment.*—The patient arrived at the Passaic General Hospital at 5 p. m., April 8. He no longer complained of pain, was comfortable and needed no relief. Morphine sulfate,  $\frac{1}{4}$  grain (0.015 Gm.), was given, nevertheless; at 6:45 p. m. the patient was seen in consultation with the surgeon (A. P. R.), who concurred in the diagnosis of a ruptured abdominal organ, and operation was decided on.

*Operation.*—At 8 p. m., with the patient under general anesthesia, a midline epigastric incision was made. An estimated 1,000 to 1,200 cc. of fresh blood was found in the peritoneal cavity. About 600 cc. of that was filtered and infused intravenously while the patient was still on the operating table. The spleen was found to have a deep tear in the anterior midportion; the splenic hilus was clamped through a left-sided oblique incision, commencing below the upper angle of the midline incision and proceeding at a 45 degree angle to it laterally for a distance of 4 to 5 inches (10 to 12.5 cm.). A normal-sized spleen was removed. Both incisions were closed in layers. A rubber drain was inserted in the midline incision, and the patient returned to his room, in poor condition.

*Postoperative Course.*—Continuous infusions of 5 per cent dextrose in isotonic solution of sodium chloride were given for forty-eight hours. On the third day an additional 500 cc. of blood was administered, and on the fourth postoperative day the condition of the patient was greatly improved and the temperature was down to 99 F. On the eleventh postoperative day, a sudden rise to 102.6 F. (39.2 C.) was observed. No cause could be found. A roentgenogram of the chest exhibited no pathologic changes, and penicillin, 600,000 units, was administered intramuscularly to the fourteenth day, when the temperature became normal. Both wounds healed without complications, and on the eighteenth postoperative day the patient was discharged from the hospital.

He continued to gain strength and weight, and on June 1 he insisted on returning to work.

*Future Course.*—He was last examined in the presence of Dr. M. Wachstein, pathologist at Beth Israel Hospital, at that institution on June 30, 1945, when a total blood count and count and smear of bone marrow and material obtained by sternal puncture were made. At that time, the patient stated that he had regained the 14 pounds (6.4 Kg.) that he had lost while hospitalized and had gained an additional 10 pounds (4.5 Kg.). He was entirely recovered.

*Laboratory Report.*—The spleen measured 12 by 10 by 7 cm., it weighed 225 Gm. and it was dark reddish purple and was slightly friable. It contained a large linear lacerated area, measuring 5.8 cm. in length and situated in its anterior midportion. The areas in the vicinity of laceration were infiltrated with extravasated blood. The splenic capsule was moderately stretched and slightly thinned. On its outer surfaces fibrous trabeculae were clearly demarcated. The malpighian



follicles were slightly obliterated in the vicinity of extravasated blood. The splenic pulp was softened in the area affected by the hemorrhage. No microscopic sections were made.

Several routine urinary analyses gave normal results. Blood counts following the operation were as follows:

|                         | 4/9/45<br>2d Post-<br>operative<br>Day | 4/19/45<br>11th Post-<br>operative<br>Day | 4/23/45<br>15th Post-<br>operative<br>Day | 6/30/45   |
|-------------------------|--|---|---|-----------|
| Total red cells.....    | 3,200,000                              | 3,100,000                                 | 4,000,000                                 | 4,320,000 |
| Hemoglobin.....         | 67%                                    | 67%                                       | 75%                                       | 81%       |
| Total white cells.....  | 17,500                                 | 32,200                                    | 7,200                                     | 9,000     |
| Polymorphonuclears..... | 88%                                    | 82%                                       | 69%                                       | 48%       |
| Lymphocytes.....        | 8%                                     | 12%                                       | 23%                                       | 45%       |

The bone marrow count revealed 70,500 cells per cubic millimeter, and the smear was normal except for 25 per cent lymphocytes. The normal is 10 per cent and the high normal 15 per cent.

#### COMMENT

A review of the literature shows that not in a single instance of spontaneous rupture of the spleen was an absolutely correct diagnosis made preoperatively or ante mortem. No single diagnostic sign, not even shock, occurred in all the cases. The site of rupture also was extremely variable, the two surfaces, the upper and lower poles, and the hilus and notch being equal favorites.

Sex and age played no part. The literature is silent on subsequent examinations of bone marrow or blood count. A hematologic study in our case revealed that while the total white cell count remained normal the lymphocyte count gradually increased from 8 to 48 per cent. Attention is invited to the bone marrow count and its 25 per cent lymphocytes, which is much higher than normal.

#### SUMMARY

A 46 year old white man, in previous good health, sustained a non-traumatic rupture of a grossly normal spleen. Splenectomy was performed within six and one-half hours after the onset of his illness. He made an uneventful recovery and was alive and well some fourteen months after the operation.

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## TESTS FOR COLLATERAL CIRCULATION IN THE EXTREMITIES

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PRIOR to the introduction of the reactive hyperemia test by Matas,<sup>1</sup> there was no method of assaying before operation whether surgical occlusion of the great arteries would be followed by relatively adequate circulation in the extremity or whether some ischemic disaster would result. Indeed such precautions are still sometimes omitted, if one is to judge by the lack of mention of any tests for adequacy of collateral circulation in a number of reports and monographs dealing with the surgery of aneurysms and arteriovenous fistulas. It is our conviction that in general the age of the patient, the duration of the aneurysm or fistula and the general appearance of the affected extremity offer nothing conclusive in regard to the safety with which ligation of the involved vessel may be carried out. It is obvious that the ideal method of treating such lesions is to restore the continuity of blood flow by some type of reparative procedure rather than by ligation of the artery. Unfortunately, in spite of the advances in the restoration of damaged arteries by suture, end to end anastomosis and vein grafts, such procedures cannot be employed in many cases and when employed, cannot be counted on to function properly and permanently in every instance. Nothing is more important, therefore, than to attempt to evaluate beforehand the efficiency of the collateral circulation.

It is the purpose of this communication to review briefly some of the tests which have been used for estimation of the adequacy of collateral circulation and to point out the value and the shortcomings of such tests. We shall discuss in more detail the tests which we have found to be practicable and helpful. We have little new to present. In a large clinical study, however, certain merits and limita-

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From the Vascular Center, Mayo General Hospital, Galesburg, Ill.

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tions in the various tests for collateral circulation have come to light. It is hoped that these may prove useful to others. Our personal experience is based on tests of collateral circulation in approximately 275 patients with arterial aneurysms or arteriovenous fistulas whom we have treated by operation. We shall deal primarily with collateral circulation in the limbs, reserving the problem of testing collateral circulation to the brain for discussion in a subsequent publication.

Tests for adequacy of collateral circulation may be divided into those which can be carried out prior to surgical exploration and those which may be utilized at the time of operation. The former are of particular importance since on them depends the rational selection of the time for operation.

#### TESTS FOR COLLATERAL CIRCULATION WHICH CAN BE CARRIED OUT BEFORE OPERATION

The first practical method of estimating the efficiency of the collateral circulation was proposed by Matas in 1910.<sup>1</sup> Moskowicz<sup>2</sup> had introduced the reactive hyperemia test as a method for determining the safe level for amputation in cases of gangrene of the extremities. This consisted essentially in completely occluding the arterial circulation in the limb by tourniquet and in observing how far distally an adequate flush prevailed after release of such occlusion. Matas convinced himself that this procedure was not a test of the level of patency of the main arterial channels, as Moskowicz had supposed it to be, but rather of adequate capillary circulation. He adapted this method as a means of estimating the efficiency of collateral circulation in cases of aneurysm. It was carried out in this fashion: The aneurysm was stilled by application of a mechanical compressor applied over the artery proximally as near the lesion as possible. Having demonstrated the manner of obliterating pulsation in the aneurysm, the compressor was temporarily released, an Esmarch bandage was applied from the distal end of the extremity to the upper pole of the aneurysm and the compressor was reapplied. The Esmarch bandage was removed after five minutes, and the compressor was left in place. The progress, extent and intensity of the flush was observed. Matas specified no limit of time for development of an adequate flush but felt that the collateral circulation might be deemed adequate if a pink color returned to the hand or foot in a reasonable time. If color did not return in an hour, for example, he felt that one should undertake obliteration of the aneurysm with extreme caution. Gradually, through the years, the standards of this test have been made more rigid. Generally an adequate flush within three minutes is considered necessary if the

2. Moskowicz, L.: Die Diagnose des Arterienverschlusses bei Gangraena pedis. Mitt. a. d. Grenzgeb. d. Med. u. Chir. 17:216-228, 1907.

collateral circulation is to be judged adequate.<sup>3</sup> We shall subsequently describe the test as we have carried it out and the standards which we have adopted.

Prior to the introduction of the reactive hyperemia test Korotkow<sup>4</sup> had suggested a test based on ionometric and sphygmomanometric movements of blood pressure in the digits during compression of the aneurysm. It was based on changes in color while the digits proximally were occluded with a manometer cuff. Matas found it unsatisfactory and abandoned it. We have had no experience with this procedure.

A test suggested by Quénu and Muret<sup>5</sup> is obviously hazardous and is mentioned only to be condemned. It consisted in cutting into the dorsal pedal artery during compression of the aneurysm to see whether bleeding would occur.

Among the three signs indicative of adequate collateral circulation suggested by von Frisch<sup>6</sup> was one which might serve as a preoperative test, namely, the persistence of normal color in hand or foot during compression of the aneurysm. This undoubtedly serves as a good index of adequacy of collateral circulation. Matas<sup>1</sup> had also utilized such observations. The chief difficulty with its execution is the maintenance of precise and complete compression of the aneurysm over a prolonged period. Often it is impossible to keep such exact occlusion of the desired portion of the artery for a long while with mechanical compressors, and with digital compression one's finger soon becomes exhausted.

The test of Tuffier and Hallion<sup>7</sup> consists in observation of venous filling in the hand or foot after the veins have been emptied by elevation of the part and then lowering of it to a horizontal level, with the aneurysm occluded by compression. As generally carried out, the limb is elevated 30 degrees until the veins are well emptied. The aneurysm is occluded by digital pressure, and the limb is lowered to a horizontal position after a blood pressure cuff at 60 mm. of mercury has been placed about the limb distal to the aneurysm. If the veins of the hand or foot fill within sixty seconds, collateral circulation is deemed

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3. Burns, Shoek, Wound Healing and Vascular Injuries, Military Surgical Manuals, National Research Council, Division of the Medical Sciences, Philadelphia, W. B. Saunders Company, 1943.

4. Korotkow, cited by Matas.<sup>1a</sup>

5. Quénu and Muret: Sur le traitement moderne des anévrismes poplités, *Rev. de chir.*, Paris **41**:282-294, 1910.

6. von Frisch, O.: Zur Indikationsstellung bei der Operation der Aneurysmen und bei den Gefäßverletzungen, *Zentralbl. f. Chir.* **41**:89-91, 1914.

7. Tuffier and Hallion: Sur un procédé permettant de prévoir que l'irrigation sanguine persistera dans un membre après ligature de son artère principale, *Compt. rend. Soc. de biol.* **73**:606, 1912.

adequate.<sup>3</sup> In discussing this test in his excellent review, Matas<sup>8</sup> stated that he found it difficult to employ because it was often rendered inaccurate by edema or venous stasis. We have found it of little practical help. Often the veins are so poorly filled, particularly in persons with pronounced vasospasm, that accurate estimation of venous filling time is impossible. In others, especially in patients with large arteriovenous fistulas, venous filling may occur promptly with compression of the fistula even while the limb is still elevated. And in others, venous stasis or edema interferes with the procedure.

Some have utilized the intradermal histamine test in order to estimate the efficiency of collateral circulation in cases of aneurysm. It is generally performed in this manner: The aneurysm is occluded by digital compression, and a drop of 1:1,000 solution of histamine phosphate is placed on the skin in the hand or foot. The skin is needled through the drop so that a wheal develops. This should appear in from three to five minutes. The prompt occurrence of a flare prior to development of the wheal is probably fully as important as the development of a wheal. Having found the histamine test not particularly helpful in the determination of the safe level of amputation in cases of gangrene, we have not utilized this test for study of collateral circulation in cases of aneurysm. The intradermal salt solution test is, in our opinion, impractical, since the wheal should persist for nearly an hour if the circulation is good and since accurate compression of the artery for such a length of time is most difficult.

If the aneurysm has brought about cessation of pulsation in the arteries distal to the lesion and if the extremity is well nourished, it may be fairly safely assumed that the collateral circulation is adequate. This observation is known as Delbet's sign.<sup>9</sup> We have found it to be useful in a number of instances. It is often present in huge subcutaneously ruptured aneurysms in which other tests for collateral circulation cannot be carried out satisfactorily because of the huge size of the aneurysm and because tenderness and pain on pressure often preclude compression of the artery. One case which may serve to question the complete reliability of the sign will be discussed subsequently.

A number of other means of estimating the efficiency of collateral circulation come to mind. We have checked the time in seconds necessary for the return of color to an area of a finger or toe blanched

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8. Matas, R.: Testing the Efficiency of the Collateral Circulation as a Preliminary to the Occlusion of the Great Surgical Arteries: Further Observations, with Special Reference to the Author's Methods, Including a Review of Other Tests Thus Far Suggested, *J. A. M. A.* **63**:1441-1447 (Oct. 24) 1914.

9. Delbet, P.: Extirpation d'un anévrisme poplité: Guérison, *Bull. et mém. Soc. de chir. de Paris* **35**:865-870, 1909.

by digital pressure and compared it with the time required for return of color without compression of the aneurysm and with the results of the same test in the normal contralateral limb. Similarly, we have milked the blood from the subpapillary venous plexus by rolling a snug rubber band from the tip of a digit to its base and checked the time for return of color after release of the constricting band during compression of the aneurysm.<sup>10</sup> Though the results from such tests as these often fit in with the deductions arrived at from the reactive hyperemia and other tests, we have not found them sufficiently helpful to continue their usage routinely. One might utilize the fluorescein test of Lange and Boyd<sup>11</sup> during compression of the artery. Our limited experience with fluorescein in determination of the adequacy of circulation in pedicle grafts and similar conditions has not been sufficiently encouraging to lead us to apply the method in cases of aneurysm. Should further studies prove its general reliability, it may be advisable to carry out such experiments in cases of aneurysm.

#### TESTS APPLICABLE AT THE TIME OF OPERATION

The test most widely known and utilized is the observation of pulsation in or free flow of blood from the distal end of the involved artery during occlusion of the proximal artery. This is known as the Coenen-Henle phenomenon.<sup>12</sup> Good retrograde pulsation in the distal artery is a comforting sign and is certainly indicative of good collateral circulation. The observation of free flow of blood can, of course, be made only after the aneurysm is opened, which is inadvisable unless one already has reasonable assurance that collateral circulation is satisfactory. Furthermore, as we shall develop subsequently, it is not a reliable indication of adequacy of collateral circulation.

Von Frisch<sup>9</sup> suggested that venous stasis below the clamped vein with the involved artery occluded was indicative of good collateral circulation. This cannot be relied on, as the tension of the vein varies not only with the efficiency of the collateral circulation but also with the state of venous filling at the time the vein is obstructed and with the adequacy of collateral venous circulation about the obstructed segment of vein.

In our experience, the most trustworthy information obtainable at the time of operation is observation of the color and warmth of the

10. Suggested by Major David I. Abramson.

11. Lange, K., and Boyd, L. J.: The Use of Fluorescein to Determine the Adequacy of the Circulation, *M. Clin. North America* 26:934-952, 1942.

12. Coenen, H.: Zur Indikationsstellung bei der Operation der Aneurysmen und bei den Gefäßverletzungen, *Zentralbl. f. Chir.* 40:1914-1916, 1913. Henle, A.: Zur Indikationsstellung bei der Operation der Aneurysmen und bei den Gefäßverletzungen, *ibid.* 41:91, 1914.

hand or foot during a prolonged period of occlusion of the involved artery. If the hand or foot maintains fairly normal color and warmth during a period of twenty to thirty minutes of temporary occlusion of the artery at the site where ligation will be necessary in order to effect a cure, one can be reasonably certain that the collateral circulation is adequate.

#### PERSONAL EXPERIENCES WITH TESTING THE COLLATERAL CIRCULATION

As mentioned in the preceding discussion, we have come to feel that the reactive hyperemia test is the most practical and reliable test which can be carried out before operation. We have employed it in the following manner: The limb is elevated. The hand is blanched thoroughly by having the patient make a tight fist. The foot is blanched by milking of the blood from the foot by the application of pressure with both hands on the dorsal and plantar surfaces and the moving of this palmar compression back toward the heel and up to the ankle. This procedure is repeated if necessary until good blanching is obtained. A similar procedure is used for hands in which motor paralysis prevents the making of a tight fist. When adequate blanching is obtained, a blood pressure cuff, previously applied about the limb distal to the aneurysm or fistula, is quickly inflated to a pressure of from 200 to 220 mm. of mercury. This provides complete interruption of arterial inflow below the level of the cuff. The hand or foot becomes extremely pale. The limb is lowered to a comfortable horizontal position. The observer has previously determined the most distal point at which digital compression of the artery completely stills the aneurysm or fistula. This is checked by palpation and auscultation, and one makes certain that such compression obliterates completely the pulsation, bruit and thrill in the aneurysm. In order to facilitate accurate observation of changes in color in the hand, foot or distal end of the extremity and at the same time of the successful obliteration of blood flow through the aneurysm or fistula, the test is always carried out by two observers. Four minutes after application of occlusive pressure in the blood pressure cuff the aneurysm or fistula is again compressed, and pressure is maintained during the remainder of the test. During this time, absence of bruit, thrill and pulsation is checked constantly by auscultation and palpation. Five minutes after the cuff has been inflated it is suddenly released, and the rapidity, completeness and intensity of the resulting flush are determined. The flush reaches the most distal portions of the extremity, the digits, if they are present, last. The number of seconds which elapse before hyperemia begins in these parts is recorded. We also

record the number of seconds which elapse before the flush becomes complete in extent and intensity. Digital compression of the artery is maintained for only two minutes after release of the blood pressure cuff. It is then noted whether there is any further improvement in the completeness or intenseness of the hyperemia. If a full and complete hyperemia occurs in less than two minutes, the collateral circulation is felt to be adequate.

Matas determined that the test could be carried out with a blood pressure cuff rather than an Esmarch bandage but felt that the latter was preferable, because he thought that its use brought about a more complete deprivation of blood and consequently a more intense reactive hyperemia. We have adopted the aforementioned method of blanching the limb and of obstructing blood flow for several reasons. In the first place, it is carried out more simply and quickly than with the use of an Esmarch bandage. In the second place, if we place the cuff somewhat distal to the aneurysm rather than bring an Esmarch bandage up to its proximal pole, we feel that it is possible by auscultation and palpation to be more certain that the aneurysm is stilled or the fistula obstructed. Compression by an Esmarch bandage is reserved for the rare instances in which adequate blanching of the limb cannot be otherwise achieved—and then it is only used to milk the blood out of the limb—while obstruction of blood flow is maintained by the inflated blood pressure cuff. We compress the artery digitally rather than by means of a mechanical compressor, since we feel that the artery can thus be more accurately occluded and with less hazard of compressing adjacent collateral vessels at the same time. The custom of having the test performed by two persons in order to permit constant and careful observation of the completeness of obliteration of the aneurysm or fistula by auscultation and palpation cannot be emphasized too strongly. Should compression be incomplete and some blood flow proceed through the compressed vessels, faulty deductions as to the efficacy of the collateral circulation might be made, with disastrous consequence.

The site of compression deserves consideration. The most distal point at which compression of the artery brings about cessation of pulsation, bruit and thrill represents that portion of the artery which opens into the aneurysmal sac or communicates with the vein or sac in instances of arteriovenous fistulas. It is at this point that the artery will have to be ligated at operation unless some reparative procedure can be carried out. Compression at some point proximal to this, though it may bring about cessation of pulsation, bruit and thrill, may give misleading information. We have attempted to illustrate this diagrammatically in figure 1. Proximal compression may occlude



blood flow through collateral vessels, which may be preserved in case operative ligation is necessary (fig. 1*A*). In such a case the test would demonstrate less adequate collateral circulation than actually exists. On the other hand, compression of the artery proximal to the aneurysm may leave open collateral channels which may necessarily have to be sacrificed at operation (fig. 1*B*). In such an instance the test would lead one to believe that the collateral circulation was better than was actually the case.

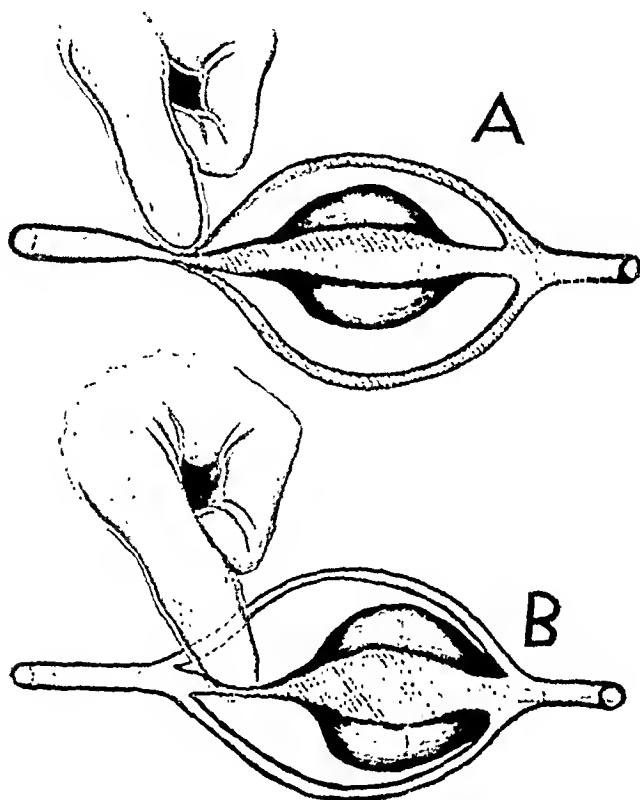


Fig. 1.—Diagrammatic representation of errors which may result from occlusion of the artery proximal to the aneurysm. In *A* an effort is made to demonstrate the possibility of occlusion of collateral channels which may be spared at operation. This would lead one to judge the collateral circulation to be less adequate than it actually was. *B* represents an effort to demonstrate the possibility of leaving open during the test collateral channels which actually arise from the aneurysm itself and must be sacrificed in extirpation of the aneurysm. If these vessels are small they may remain open, and yet at the same time pulsation and bruit may be absent. Such an occurrence might lead one to feel from the test that the collateral circulation was better than was actually the case.

One problem of considerable importance concerns the basal conditions under which the test is carried out. Reactive hyperemia is better when the limb tested is in a state of vasodilatation rather than of vasoconstriction. In the absence of sympathetic denervation, limbs in

which aneurysms or arteriovenous fistulas occur are capable of a wide variation in vascular tonus, just as are normal limbs. Should the test be carried out under ordinary conditions and at the ordinary temperature of the ward or under conditions conducive to vasoconstriction or vasodilatation? We have repeatedly demonstrated significant difference in the results of the reactive hyperemia test under ordinary conditions in a ward, during extreme vasoconstriction and during full vasodilatation, by repeating the test on a given patient under these varying conditions on the same day. In general, the test shows evidence of poorer collateral circulation during vasoconstriction and of better collateral circulation during vasodilatation. Since the patient is destined to live in the environment of a ward after operation and since constant maintenance of full vasodilatation cannot be assured unless sympathectomy is performed, it is our feeling that the procedure is best carried out without effort to induce either vasoconstriction or vasodilatation.

There are certain errors which occasionally enter into the test and result in inaccurate estimation of the efficiency of the collateral circulation. These errors prevail in all tests which depend on compression of the involved segment of artery. In the first place, this may result from improper localization of the lesion or, to express it in another manner, from simultaneous compression of an uninvolved main arterial stem during compression of the affected minor artery. For example, in a 24 year old patient with a five month old arteriovenous fistula in the popliteal fossa, pressure sufficient to obliterate the bruit and thrill invariably resulted in loss of pulsation in the dorsal pedal and posterior tibial artery and study of collateral circulation gave results suggesting entirely inadequate collateral circulation. Repetition of these tests showed no improvement with the passage of time and with intermittent occlusion of the fistula by compression. Five weeks after admission a lumbar sympathectomy was performed, after which the flush during the reactive hyperemia test was prompter and of greater intensity. Six weeks after operation the collateral circulation was judged to be adequate and operation was done. On exploration, the fistula was found between the inferior geniculate artery and the overlying popliteal vein rather than between the popliteal artery and vein, as had been suspected beforehand. The fistula was so close to the popliteal artery that it could not be occluded by digital compression without occlusion also of the popliteal artery. The fistula was easily excised without disturbing the popliteal artery. We have attempted to illustrate our experience with tests for collateral circulation on this patient in figure 2.

Similarly, another 24 year old patient, with signs of an arteriovenous aneurysm of four months' duration in the sternoclavicular region, lost

his brachial and radial pulse during each compression of the fistula. Again collateral circulation was judged inadequate according to all studies. After four weeks of further observation and intermittent compression, he was subjected to dorsal sympathectomy, following which the reactive hyperemia test indicated good collateral circulation. At operation the fistula was found between the transverse cervical artery and the proximal end of the internal jugular vein instead of between the subclavian vessels, as we had anticipated. The fistula could be excised without interference with the subclavian vessels. Had

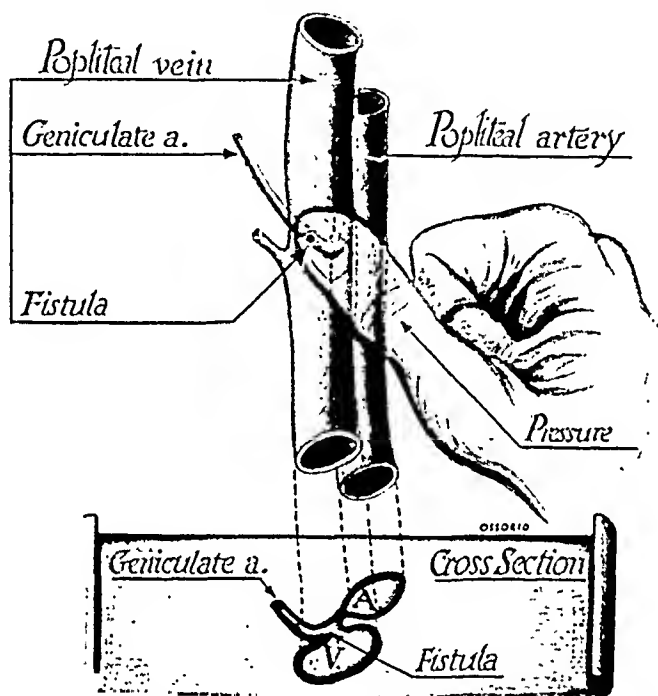


Fig. 2.—Semidiagrammatic drawing of the findings in a patient with a fistula between geniculate artery and popliteal vein. It was impossible to compress the fistula without at the same time occluding the adjacent popliteal artery.

it been possible to compress the fistula itself in these 2 cases without also compressing a more important adjacent artery, both of the patients might have had correct localization before operation and might have been spared sympathectomies. Lesions in the proximal portion of the profunda femoral vessels constitute one of the most difficult problems in correct localization of fistula or aneurysm and in correct testing of the collateral circulation. In order to obliterate the fistula or still the aneurysm by direct pressure, almost invariably the overlying superficial femoral artery must be compressed, with resultant error in localization and in interpretation of the efficacy of collateral circulation.

Conversely, if one can definitely establish the fact that the lesion is in a minor vessel and can demonstrate that pulsation, bruit and thrill can be eliminated by pressure, with preservation of blood flow in the main arterial stems, one has little worry concerning the nutrition of the part following excision. Often careful repeated examinations will enable one to make correctly such a localization even when the lesion is near the main artery. For example, in patients who presumably have axillary arteriovenous fistulas or aneurysms, it is often possible to demonstrate that the lesion actually involves the thoracoacromial trunk, the subscapular vessels or other branches. A word of warning, however, is necessary in this regard. In a single instance, the lesion involved not only a minor branch but also the main artery. The patient was a 41 year old soldier who had an arteriovenous fistula, of six months' duration, which was thought to involve one of the circumflex humeral vessels. The bruit and thrill could be eliminated by direct pressure without disturbing the brachial pulse. At operation it was found not only that the anterior circumflex humeral artery and vein communicated through a small sac but that the superior portion of the axillary artery opened into this sac through a large fistula. It had been possible to compress the sac in such a manner that the openings from the two arteries and the vein were occluded without compression of the axillary artery itself. Ligation was necessary because the damage to the axillary artery was too extensive to permit repair. Consequently, the efficacy of the collateral circulation had to be established during the operation by observation of the color and warmth of the hand during prolonged temporary occlusion of the axillary artery with a rubber-shod clamp.

Another manner in which the tests may indicate a poorer collateral circulation than actually exists is through the inadvertent compression of collateral channels which are actually uninvolved and can be spared during operative excision of the lesion. In our experience this has apparently occurred chiefly from transmission of pressure through the laminated thrombus in a saccular aneurysm. We have attempted to illustrate this in figure 3. It is exemplified by the following case: A 20 year old patient with a traumatic popliteal arterial aneurysm of three months' duration had inadequate flush during the reactive hyperemia test. He had no significant improvement in this test during the next five and one-half weeks. Lumbar sympathectomy was performed, following which the test indicated somewhat better but still inadequate collateral circulation. After repeated observations the aneurysm was explored, approximately eight months after the initial injury. It was explained beforehand to the patient that if during temporary occlusion of the artery at the site of the aneurysm the foot should show ischemic

changes nothing more than a partial proximal ligation could be done. At operation it was found that the artery could be occluded over a prolonged period, with maintenance of good color and warmth in the foot. The aneurysm was large and contained an extensive laminated thrombus. It was apparent from its character and position that pressure on the artery sufficient to still the aneurysm had occluded the geniculate branches by transmission of pressure through the wall of the aneurysm. The aneurysm was excised, with ligation of the involved artery and with preservation of the geniculate branches. The patient maintained a warm, well colored foot.

The same error in interpretation of the collateral circulation may result from the presence of collateral channels in such a position that the aneurysm cannot be stilled by pressure without also directly compressing the collateral vessels. Our experience with a 23 year old soldier who had a traumatic axillary arterial aneurysm of three months'

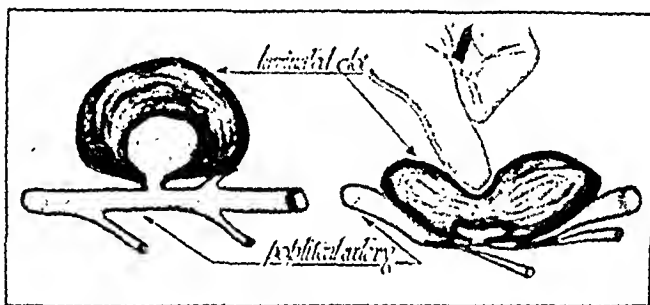


Fig. 3.—In this drawing we have attempted to illustrate the occlusion of uninvolved collateral channels by transmission of pressure through the laminated thrombus within the sac. In such cases preoperative tests indicate poorer collateral circulation than actually exists.

duration illustrates this mechanism. He had a large aneurysm in the third portion of the axillary artery and pronounced impairment of function of the brachial plexus. His collateral circulation was inadequate as judged by the reactive hyperemia test. Because of the damage to the nerves, it was felt advisable to do everything possible to render the collateral circulation adequate so that operation could be carried out as soon as possible. Three weeks after admission a dorsal sympathectomy was performed, and intermittent digital compression was given from time to time. The reactive hyperemia test continued to reveal evidence of insufficiency of collateral circulation. With the patient's understanding that nothing more than partial proximal ligation might be feasible, the aneurysm was explored approximately two months after sympathectomy. With direct visualization it was understandable why the test for collateral circulation had indicated insufficient collateral circulation. The aneurysm was large. The radial, ulnar, and median

nerves were stretched over the surface of the sac and were compressed by it. There was a large collateral artery which emerged proximally from the axillary artery and passed directly over the aneurysmal sac only a few millimeters away from the involved portion of the axillary artery. It was apparent that compression sufficient to still the aneurysm would have also necessarily interrupted blood flow through this large collateral channel. The hand remained warm and of excellent color during prolonged temporary occlusion of the axillary artery with a rubber-shod clamp. The aneurysm was excised, and appropriate operation for the injuries to the peripheral nerve of the patient was carried out. The collateral vessel mentioned was saved. It was possible to excise the damaged portion of the axillary artery and reconstruct it by means of end to end suture.

Thus far we have discussed errors in testing which might lead to the impression that the collateral circulation is poorer than it actually is. Such errors are troublesome. They cause an unnecessary delay in operative cure of the aneurysm and untold worry to the surgeon. Nevertheless, if properly handled, they will not jeopardize the involved limb. The contrary is obviously true in case an error in testing efficiency of collateral circulation leads to the false assumption that it is adequate. A single instance of this sort has occurred in our experience, the only case in which operative excision of an aneurysm has been immediately followed by obviously insufficient circulation with steady death of tissue and ultimate gangrene of the distal third of the foot. The patient was a 35 year old soldier who had a popliteal arteriovenous fistula of two and one-half months' duration. There was practically no flush of the foot during the reactive hyperemia test performed under ordinary conditions, but there was a great deal better flush during reflex vasodilatation. Three weeks after admission a lumbar sympathectomy was carried out, following which there was a good flush during the test. The popliteal vessels were explored about four months after the patient had sustained his injury. Immediately prior to operation he had shown a good hyperemia which began in his toes in twenty seconds and became complete in exactly two minutes. The condition found at operation is illustrated in figure 4. Not only was there a direct communication between the popliteal artery and vein, but there was a saccular arterial aneurysm as well and a large geniculate artery emerged from the aneurysmal sac proximal to the fistula. It seemed entirely likely that digital compression had occluded the fistula and had not occluded blood flow through this geniculate artery. In order to remove the aneurysm it was necessary, however, to sacrifice this vessel. This was done, the involved segment of the artery and vein being excised. The postoperative course has

been described. It was felt that in all likelihood misleading information had been obtained from the reactive hyperemia test.

Since the patient had shown what we thought to be a good and complete flush just two minutes after release of the constricting blood pressure cuff during the reactive hyperemia test and had suffered such an ischemic disaster following excision, we felt it necessary to revise our standards of this test. Up to this time, we had considered an intense

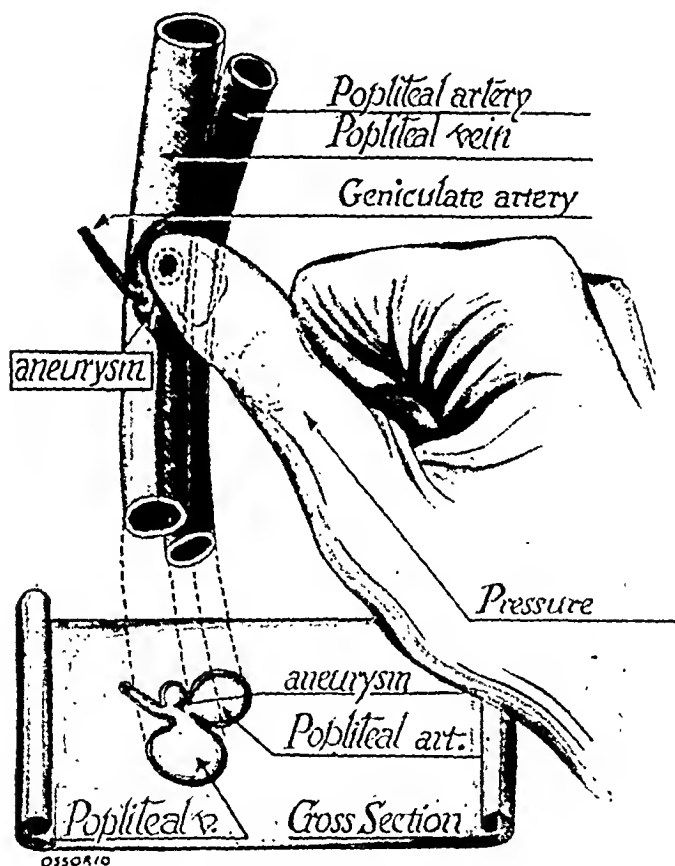


Fig. 4.—In this drawing an effort is made to depict the findings in a patient in whom the collateral circulation was judged better than it actually was. In all likelihood, digital compression occluded the fistula successfully but left open a large geniculate branch which emerged from the aneurysmal sac and had to be sacrificed in extirpation of the aneurysm.

and complete flush within three minutes as evidence of satisfactory collateral circulation. Since then, we have felt that a full, complete flush must prevail in less than two minutes, with no further significant improvement on release of pressure from the artery, before the collateral circulation is considered to be adequate.

This patient illustrated another most important point. Since we had felt that the collateral circulation was adequate from the preoperative

tests, his feet were not draped so that they could be observed during the operation. Had this precaution been taken and the color and the warmth of the feet been observed during temporary occlusion of the involved vessels below and above the site of the fistula, we should undoubtedly have noticed changes in color and perhaps temperature which would have made it apparent that excision of the lesion should be deferred. Since that time it has been our policy to expose the hand or foot in every instance in which there is the slightest question as to the adequacy of collateral circulation and to make certain that the color and warmth of the part remain good during prolonged occlusion of the involved artery with a rubber-shod clamp. This experience further illustrates the previously mentioned fact that the free flow of blood from the distal artery is not necessarily a definite sign that collateral circulation is adequate, for at operation the patient had fairly good retrograde bleeding from, although no pulsation in, the distal end of the artery.

It is important to inquire whether any evidence which testifies to the validity of the reactive hyperemia test has been accumulated. This is a most important question and one which is exceedingly difficult to answer on the basis of clinical experience. Certain observations, however, suggest that the test is generally reliable though not infallible. In the first place, with one exception previously mentioned and with a second possible exception to be discussed subsequently, all the patients who have had tests suggesting adequate collateral circulation have maintained excellent circulation following operative obliteration of the aneurysm or fistula. In the majority of these patients, the involved artery was ligated. They have maintained good warmth and color of the extremity and have not had, even for a brief period, any sensory or motor loss or other evidence of ischemia. In the 1 instance of gangrene, previously described, the findings at operation suggested a possible adequate explanation for the misleading information derived from the preoperative test.

In the second place, some confirmation of the validity of this test is obtained from experience with the patients who had evidence of inadequate collateral circulation at the time that the aneurysm was cautiously explored. In all but 1 of these patients, study of the circulation in the hand or foot during a prolonged period of temporary occlusion of the artery revealed evidence of adequate collateral circulation. In the great majority there prevailed some anatomic situation which offered a reasonable explanation of the misleading preoperative reactive hyperemia tests. Certain of the anatomic mechanisms involved have been discussed.

In the third place, some more precise information concerning the accuracy of the test is derived from our experience with 2 patients.



The first was a 37 year old man who had a traumatic arterial aneurysm of the proximal portion of the popliteal artery. Reactive hyperemia study showed practically no flush. Up to this point our experience with increasing the efficacy of collateral circulation by means of sympathectomy had been so uniformly successful that at the time we held too optimistic a view concerning its value. The aneurysm was consequently explored, and its cure necessitated ligation of the artery. The foot was cold and blue following this procedure and was much the same following a sympathectomy which was performed immediately after excision of the aneurysm. The foot remained rather cold for several hours, and then the color and warmth returned to normal. However, during this interval of ischemia, ischemic nerve paralysis had developed, which weakened all the movements of his foot and paralyzed extension and which resulted in hypesthesia or anesthesia of the distal third of the leg and foot. Fortunately he recovered satisfactorily from this disability. This ischemic difficulty following operation in the face of poor reactive hyperemia tends to confirm the reliability of this test. The second patient was a 27 year old man with a femoral arteriovenous fistula. Three and one-half months after injury a lumbar sympathectomy was performed, because the reactive hyperemia test showed practically no flush. This study, frequently repeated after sympathectomy, continued to indicate poor collateral circulation. This was not altered by frequent intermittent occlusion of the artery. The aneurysm was explored six months after injury, and at the time of operation the involved segment of the artery was occluded with a rubber-shod clamp. The foot immediately became pale and after some minutes was completely white. The wound was closed without excision of the aneurysm. This confirmation on the operating table of the poor collateral circulation also serves to establish the validity of the reactive hyperemia test.

These observations all tend to confirm the reliability of the reactive hyperemia test. It must be stated, however, that exploration has been carried out in a few instances in which nothing was found at operation to explain the discrepancy between a poor preoperative test and the actual presence of adequate collateral circulation. In these few cases preoperative study had indicated poor or questionable collateral circulation. During the precise temporary occlusion of the involved artery at operation, excellent color and warmth had been maintained in the hand or foot and excision of the lesion with ligation of the artery was followed by good circulation. These cases are few but are important, since they reveal the fact that the reactive hyperemia test as we have employed it is not infallible. We conclude that this procedure is practical and helpful, though sometimes misleading. It would be most desirable to

check the reliability of this test in experimentation on animals, in which accurate controls would permit more convincing deductions.

We have mentioned beforehand that numerous other tests for collateral circulation have been utilized which are not considered sufficiently helpful to warrant their routine use, though they often confirm the reactive hyperemia test. Two observations have, however, been found to be helpful. The first is the observation of the color and warmth of the hand or foot during prolonged compression of the involved artery. We have referred to the difficulties involved in carrying out this test properly. In the interpretation of the results of this study, it is important to assay the circulatory status of the hand or foot in positions other than the horizontal one. We have found pronounced pallor of the hand on elevation when the color and warmth remained excellent in the horizontal position during a period of thirty minutes of compression. The second is Delbet's sign. We have seen nothing to suggest that if the arterial pulses have been lost in an extremity distal to an aneurysm and the limb has maintained good circulation ligation of the artery entails any hazard of ischemic difficulty. We have studied 1 patient who had definite evidence of impaired circulation in a limb in which all pulses distal to a large subcutaneously ruptured femoral aneurysm were absent. The patient had lost tibial and saphenous sensation, though no motor function. He was in great pain. A sympathectomy was performed, following which the previously poor reactive hyperemia was excellent. Aneurysmorrhaphy, with ligation of the artery, was immediately performed. After operation, the foot maintained excellent color and warmth but some peroneal sensory loss was added to the existing sensory difficulty. Motor function remained intact. Because of the excellent color and warmth of the foot, it was hard to explain this added sensory difficulty on an ischemic basis. Conceivably, further damage to the already injured sciatic nerve may have resulted from the temporary use of a tourniquet. Difficult as this complication is to explain, it is cited as an example of postoperative sensory loss, possibly on an ischemic basis, in a limb having evidence of impaired circulation and no pulses distal to the aneurysm.

With regard to the tests applicable at the time of operation, we have previously commented on the probable reliability of good retrograde pulsation in the distal artery, the unreliability of retrograde bleeding without retrograde pulsation and the errors inherent in interpretation of venous stasis below the clamped vein during occlusion of the involved artery. In our experience the most reliable sign is the maintenance of relatively good color and warmth of the hand or foot during occlusion of the involved segment of artery with a rubber-shod clamp. This observation should, we feel, extend over a period of at least twenty,

and preferably thirty, minutes. It should be emphasized that if the operation is performed with the patient under spinal or general anesthesia this test indicates adequacy of collateral circulation during inhibition of vasoconstrictor impulses. Conceivably the collateral circulation might not be satisfactory if vasoconstriction should occur. If an aneurysm or fistula is treated and ligation of the artery is performed on the basis of such an observation, one should be prepared to eliminate sympathetic impulses should circulation be subsequently compromised by vasoconstriction.

Finally, it should be stated that all the tests which have been discussed are based on the assumption that the existing collateral channels will remain patent. Should they be occluded subsequently by thrombosis, disaster may occur. We have had the misfortune to have one example which illustrates this difficulty. A 25 year old patient with a femoral arteriovenous fistula had evidence of good collateral circulation. Eight and one-half months after injury the fistula was explored. While the involved segment of the artery was occluded with a rubber-shod clamp, the foot maintained good color. The fistula was excised, with ligation of the femoral artery just below the point where the profunda originates. The circulation in the foot was satisfactory until the sixth postoperative day, when pain suddenly developed in the popliteal space, calf and foot, and pronounced hypesthesia of the foot developed. Subsequently edema developed, and it was apparent on examination that the patient had undergone thrombosis of some of the arterial collateral vessels and extensive thrombosis of the deep veins of the calf. Within a few hours after this accident, a sympathectomy was performed. Despite the fact that it improved the circulation somewhat, gangrene of the toes and sole developed, necessitating amputation.

#### COMMENT

The determination of the adequacy of collateral circulation prior to exploration for aneurysm or arteriovenous fistula is most important. We feel that the most reliable and practical preoperative test for collateral circulation is the reactive hyperemia test. Though of great practical help and general reliability, this test is not infallible. The chief difficulties arise from the occasional impossibility of accurate compression of the involved arteries at the exact site of the fistula or aneurysm without concomitant compression of neighboring uninvolved vessels. If an excellent and complete flush occurs promptly during the test, with no further improvement on release of the compressed artery, one may approach the aneurysm and ligate, if necessary, the involved artery, with minimal risk of ischemic difficulty.

If the reactive hyperemia test indicates borderline or poor collateral circulation, every effort should be made to bring about improvement in the collateral circulation prior to exploration. If one does not succeed in establishing collateral circulation which is adequate according to this test, exploration should be carried out with great caution. The hand or foot should be exposed during operation and should be observed for change in color and temperature during prolonged temporary occlusion of the involved segment of artery. If ischemia of the hand or foot prevails, extirpation of the lesion should be deferred unless it is perfectly evident that a cure can be effected with maintenance of continuity of the involved artery.

Continued good circulation in the extremity during prolonged compression of the involved segment of artery is a somewhat difficult but useful confirmatory preoperative test. The absence of pulses distal to an aneurysm or fistula in a limb which maintains good circulation is indicative of adequacy of the collateral circulation.

All preoperative study of collateral circulation is based on the premise that no collateral vessels will be needlessly destroyed during operation and that no postoperative thrombosis will occur.

Though present methods of study render operation on aneurysms fairly safe, it is hoped that future investigation will produce more precise means of estimating collateral circulatory adequacy.

#### SUMMARY

Various methods for testing the efficiency of collateral circulation have been reviewed, and those which we have found most useful have been discussed in detail. An effort has been made to point out the utility of these procedures and at the same time to indicate their pitfalls and limitations.

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## EFFECT OF PENICILLIN IN EXPERIMENTAL INTESTINAL OBSTRUCTION

Cure of Strangulated Ileal Obstructions Treated with Penicillin  
Prior to Late Resection

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**E**XPERIMENTAL evidence for the importance of the role played by bacteria in producing "toxemia" and death in intestinal obstruction is briefly as follows: Dogs having isolated obstructed jejunal loops will die from a rather characteristic train of symptoms within a few days, usually four or five.<sup>1</sup> When penicillin is either placed in such loops or administered parenterally to dogs in which such loops have been constructed, these dogs will be protected from "toxemia" and death for a significant period, sometimes for over a month.<sup>2</sup> Succinyl-sulfathiazole, which is absorbed more slowly from isolated loops, will also protect animals with isolated obstructed loops when placed in the loops at the time of operation.<sup>3</sup> One such dog was allowed to survive for over a year.<sup>3b</sup> Prior to the advent of potent antibacterial drugs for experiments of this type, the importance of bacteria as the cause of death was strongly suspected on the basis of a process of exclusion by such investigators as Davis and Stone,<sup>4</sup> Murphy and Brooks<sup>5</sup>

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From the Surgical Hunterian Laboratory of the Johns Hopkins University School of Medicine and the Johns Hopkins Hospital.

1. Stone, H. B.; Bernheim, B. M., and Whipple, G. H.: Intestinal Obstruction: A Study of the Toxic Factors, *Bull. Johns Hopkins Hosp.* **23**:159-165 (June) 1912.

2. Harper, W. H., and Blain, A., III: The Effect of Penicillin in Experimental Intestinal Obstruction: Preliminary Report on Closed Loop Studies, *Bull. Johns Hopkins Hosp.* **76**:221-244 (June) 1945.

3. (a) Poth, E. J., and Firor, W. M.: Unpublished data. (b) Harper, W. H., and Blain, A., III: Unpublished data.

4. Davis, D. M., and Stone, H. B.: Studies on the Toxicity in Intestinal Secretion, *J. Exper. Med.* **26**:687-691 (Nov.) 1917.

5. Murphy, F. T., and Brooks, B.: Intestinal Obstruction: An Experimental Study of the Causes of Symptoms and Death, *Arch. Int. Med.* **15**:392-412 (March) 1915.

and, especially, Dragstedt.<sup>6</sup> In 1944, the efficacy of prophylactic succinylsulfathiazole in protecting dogs having ileal lesions produced by occlusion of mesenteric veins but in which the lumen of the bowel was not obstructed was reported.<sup>7</sup>

In a recent communication by Blain and Kennedy<sup>8</sup> experiments demonstrating the striking but limited protection afforded by massive doses of penicillin in dogs with strangulated obstructions of the lower part of the ileum were described.

This present report is concerned with an account of 5 dogs in which resection of a strangulated ileal obstruction was performed at a period twice as long after the production of the strangulation as any control dog, not treated with penicillin, lived. Four of these resections were completely successful, and the dogs were cured. Two of the dogs in which resections were performed, as well as their controls, were mentioned previously.<sup>3</sup>

#### EXPERIMENTAL METHODS

The details of the experimental procedures utilized in these studies were given in the previous report by Blain and Kennedy.<sup>8</sup> The fundamental steps were as follows: Strangulated obstruction in each of 5 control dogs and 5 treated dogs was produced in the following manner. With the animals under anesthesia induced by pentobarbital sodium given intravenously, a right rectus incision was made, and through this the terminal part of the ileum was delivered. At a point just proximal to the termination of the antimesenteric artery the bowel was transected between clamps, and each of the two ends was inverted by the closed method of Parker and Kerr. The mesenteric veins to a 60 cm. segment of the proximal part of the ileum were occluded with double silk ties, as were the arteries and veins running parallel to the bowel toward the selected segment. At either end of the segment to be strangulated, the mesentery was divided down to its base in order to preclude the development of any collateral venous channels.

All dogs were starved for twenty-four hours prior to operation, and food and fluids given orally were withheld postoperatively until after the second operation (resection and anastomosis), which was performed in the dogs treated with penicillin. Cultures of the lumen bowel were made in dogs to be treated with penicillin. At autopsy of all the dogs which died, cultures were taken of the obstructed bowel, the heart blood and the peritoneal transudate which developed as a result of the strangulation. In all cases the strangulated segment of ileum measured at least 50 cm. at the end of the operation, and in all cases this segment

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6. Dragstedt, L. R.; Moorehead, J. J., and Burcky, F. W.: Intestinal Obstruction: An Experimental Study of the Intoxication in Closed Intestinal Loops, *J. Exper. Med.* **25**:421-439 (March) 1917.

7. Sarnoff, S. J., and Poth, E. J.: Intestinal Obstruction: I. The Protective Action of Succinylsulfathiazole Following Simple Venous Occlusion, *Surgery* **16**:927-931 (Dec.) 1944. Sarnoff, S. J., and Fine, J.: The Effect of Chemotherapy on the Ileum Subjected to Vascular Injury, *Ann. Surg.* **121**:74-82 (Jan.) 1945.

8. Blain, A., III, and Kennedy, J. D.: The Effect of Penicillin in Experimental Intestinal Obstruction: Studies on Strangulated Low Ileal Obstructions, *Bull. Johns Hopkins Hosp.* **79**:1-20 (July) 1946.

was cold and black or deep purple and had begun to exude sanguinous fluid when returned to the abdomen. At autopsy or at the operation for resection the affected segment was always found to be black or dark purple, heavy and edematous and distended and stretched, so that it measured at least 70 cm. in length, and its walls showed varying degrees of necrosis.

Immediately following the operation in which obstruction and strangulation were produced, each dog was given 500 cc. of whole blood intravenously and 500 cc. of isotonic solution of sodium chloride subcutaneously. Prior to operation blood was taken for a determination of the hematocrit level. This was repeated at intervals after operation, and a fall of 5 degrees in the hematocrit content was regarded as sufficient indication for additional administration of whole blood. If the hematocrit level rose or if the animal vomited, additional isotonic solution of sodium chloride was administered. Seven per cent gelatin was kept in readiness in case the hematocrit content continued to rise in spite of the administration of isotonic solution of sodium chloride. In some of the dogs occasional direct measurements of the systolic blood pressure were made.

In the 5 dogs receiving penicillin, the dosage for this drug was as follows: 100,000 units every two hours during the first twenty-four hours, beginning from between one-half hour to three hours postoperatively, 50,000 units every two hours during the next forty-eight hours and 50,000 units every two hours for the twenty-four hour period following the second operation. Thus the total dosage for each of these 5 dogs in the first twenty-four hours after the beginning of treatment was 1,200,000 units and by the end of the first seventy-two hours 2,400,000 units. The total dosage was 3,600,000 units in ninety-six hours. The relative magnitude of such a dosage schedule can be appreciated when it is pointed out that the weights for these 5 dogs averaged only a little over 33 pounds (15 Kg.). At autopsy on the control dogs, which was performed immediately after death, cultures were made, as mentioned, and the strangulated obstructed segment low in the ileum was removed, measured, photographed and then placed in solution of formaldehyde, along with sections of the major organs. This same procedure was followed in the penicillin-treated dogs at the operation for resection. Microscopic sections of tissues removed at autopsy were made, and bacterial stains were done on all sections of the intestine.

Blood specimens of all dogs were taken just before or immediately after death, for determinations of chloride and hematocrit levels. In addition, in some of the dogs other determinations such as the nonprotein nitrogen, total serum protein, calcium, phosphorus, sodium, potassium and carbon dioxide-combining power were made.

## RESULTS

*I. Control Dogs.*—The survival time for the 5 control dogs ranged between twenty-six and a half hours and thirty-six hours (chart 1). The determinations of hematocrit levels and the fluids administered to each dog are plotted in table 1. A sixth dog, intended for the control series, showed at autopsy strangulation of the proximal turned-in end, with leakage of intestinal contents into the peritoneal cavity, and was excluded from the series. The symptomatology, which was the same in each of these dogs, has been described in detail.<sup>8</sup> Briefly, they were usually awake and standing in their cages in from two to ten hours; within four to sixteen hours postoperatively they had vomited bloody, foul-smelling material, which was at first bright red and later

a dark brownish red. The amount and severity of the vomiting varied, and the amount of isotonic solution of sodium chloride given subcutaneously varied accordingly. Ascites, which was always bloody at autopsy, became clinically evident within five hours after operation. Often large, distended loops of bowel were both palpable and visible beneath the wall of the abdomen. Borborigmi were audible and violent peristaltic movements visible. The animals died in a remarkable manner. In some cases they would appear to be in relatively good condition and would extend their legs, gasp and die. In other cases (3) there was a terminal "toxic" phase, lasting from twenty minutes to seventy minutes. This phase was marked by severe retching and vomiting while the dog was erect, followed by a slumping to the prone position. At this stage, all four legs were paralyzed and the animal would collapse if an attempt was made to stand it up. Soon the animal would become comatose, and it would die within a few minutes after extending its legs. In all animals death was rapid and not at all characteristic of the slow deaths of dogs dying in shock. In only 1 of the 5 dogs was a gross perforation of the strangulated bowel observed at autopsy, and this was through a large, round mucosal ulcer located on the mesenteric border of the bowel. This is in pronounced contrast to 10 controls reported on,<sup>8</sup> in 5 of which bowels were perforated, and in these the perforations were antimesenteric in location. The bowel contained old, foul-smelling blood in all cases. The peritoneal cavities contained between 500 and 2,000 cc. of bloody transudate having the composition of blood serum and a hematocrit level of around 15. The strangulated segments showed gross and microscopic evidence of ulceration, necrosis of the intestinal wall and pronounced hemorrhage into the wall. There was always pronounced ulcerative diphtheritic enteritis and also infection of the damaged and necrotic wall. Bacterial stains revealed the presence of many types of bacteria, both gram-positive and gram-negative, in the intestinal wall.

*II. Dogs Treated with Massive Doses of Penicillin.*—Of the 5 dogs treated with massive doses of penicillin included in this report, all lived seventy-two hours, at which time resection of the strangulated segment was carried out. There was a sixth dog treated with penicillin, which died in under twenty-nine hours and which at autopsy proved to have strangulation of the proximal turned-in end. This end leaked bowel contents into the peritoneal cavity, and as a result this animal was excluded from the series.

As is illustrated in the chart, 1 of the dogs died eight hours after resection of its strangulated bowel. This dog was "toxic" for perhaps an hour prior to operation. It was retching and vomiting strenuously, and it had a rapid thready pulse. At the time at which resection was performed the dog was still standing and had not yet become comatose.







determinations of hematocrit levels and the fluids administered to the dogs given penicillin and then resected are plotted in table 1. Microscopic sections of the strangulated bowel removed revealed necrosis and pronounced hemorrhage into the intestinal wall, ulceration and infection. Bacterial stains revealed the presence of many types of bacteria, both gram-positive and gram-negative. In many sections the number of bacteria was definitely less than in similar sections of strangulated bowel from control dogs.

#### CHEMICAL STUDIES

It was found, as was expected, that in the dogs which died there was terminally a rise in the serum nonprotein nitrogen. The values for phosphorus and potassium were high. The values for chloride and sodium were within the normal range or above it. The carbon dioxide values were low and indicated the presence of acidosis.

*Bacteriologic Studies.*—The organisms most frequently encountered in the intestinal tract were *Escherichia coli*, *Streptococcus faecalis*, *Staphylococcus aureus* and *Clostridium welchii*. *Pseudomonas aeru-*

TABLE 2.—*Fluid Therapy in Paired Dogs over Equal Units of Time*

The total fluids for the control dogs during their survival and the fluids given corresponding penicillin-treated dogs (see table 1) for comparable periods are listed. The dogs were paired thus: 86 and 95, 89 and 97, 111 and 107, 112 and 108 and 113 and 109.

|   | Five Control Dogs | Five Treated Dogs |
|---|-------------------|-------------------|
| Blood.....                                | 7,750 cc.         | 7,500 cc.         |
| Isotonic solution of sodium chloride..... | 10,750 cc.        | 6,250 cc.         |
| Total.....                                | 18,400 cc.        | 13,550 cc.        |

ginosa and *Proteus vulgaris* were also occasionally grown. Rarely one organism would overgrow the others to produce a pure culture. The peritoneal cultures were often sterile during the first twenty-four hours, whether or not the dogs were treated with penicillin, unless perforation had occurred.<sup>8</sup> All specimens of heart blood in this series were sterile.

*The Factor of Shock.*—There was often a diminution in the systolic blood pressure, but it is believed that no dog in this series died of shock. This subject was discussed fully previously.<sup>8</sup> It can be seen in table 2 that the control dogs were treated as vigorously for shock, hemorrhage, chloride and loss of water as were the penicillin-treated dogs.

#### COMMENT

Great strides have been made in reduction of the mortality rate associated with acute intestinal obstruction. This mortality rate has been brought down from around 60 per cent<sup>9</sup> to as low as 15 to 20 per

9. Miller, C. J.: Study of Three Hundred and Forty-Three Surgical Cases of Intestinal Obstruction, *Ann. Surg.* 89:91-107 (Jan.) 1929.

cent.<sup>10</sup> In one recent series<sup>11</sup> the mortality rate was reported to be 8 per cent. The chief factors responsible for this improvement, aside from more modern surgical technic and better methods for the management of shock, were the introduction of methods for the relief of distention by intubation and suction<sup>12</sup> and advances in knowledge concerning electrolyte and water balance.<sup>13</sup>

This progress, although representing a great victory in the treatment of an important surgical condition, has not yet reached a point where the results of treatment can be regarded with complacency. The so-called conservative school of management of intestinal obstruction is represented by surgeons who prefer to try to differentiate on clinical evidence between strangulated and nonstrangulated obstructions. This is done so that operation may be delayed in the cases of nonstrangulated obstruction for purposes of decompression and replacement of fluid. Those who adopt such a conservative regimen must not overlook the fact that early strangulation is difficult if not impossible to diagnose accurately short of direct visualization of the affected bowel wall. Furthermore, the factor of strangulation is the most important single factor in determining the outcome of a case of acute obstruction.<sup>14</sup> Because of the efficacy of penicillin in experimental strangulated obstructions,<sup>8</sup> a trial of massive doses of penicillin has been advocated by Calihan,

10. Calihan, R. J.; Kennedy, J. D., and Blain, A., III: Intestinal Obstruction: A Study of Two Hundred and Four Acute Cases with Reference to the Possible Efficacy of Anti-Bacterial Therapy, *Bull. Johns Hopkins Hosp.* **79**:21-33 (July) 1946.

11. Moses, W. R.: Acute Obstruction of the Small Intestine: A Report of One Hundred and Eighteen Cases, *New England J. Med.* **234**:78-81 (Jan. 17) 1946.

12. Abbott, W. O., and Johnston, C. J.: Intubation Studies of the Human Small Intestine, *Surg., Gynec. & Obst.* **66**:691-697 (April) 1938. Johnston, C. G.: Decompression in the Treatment of Intestinal Obstruction, *ibid.* **70**:365-367 (Feb.) 1940. Wangenstein, O. H.: *Intestinal Obstructions*, ed. 2, Springfield, Ill., Charles C Thomas, Publisher, 1942.

13. Hartwell, J. A., and Hoguet, J. P.: Experimental Intestinal Obstruction in Dogs with Especial Reference to the Cause of Death and the Treatment by Large Amounts of Normal Saline Solution, *J. A. M. A.* **59**:82-87 (July 13) 1912. McLean, A., and Andries, R. C.: Ileus Considered Experimentally, *ibid.* **59**:1614-1617 (Nov. 2) 1912. Haden, R. L., and Orr, T. G.: Effect of Sodium Chloride on the Chemical Changes in the Blood of the Dog After Pyloric and Intestinal Obstruction, *J. Exper. Med.* **38**:55-71 (July) 1923. MacCallum, W. G.; Lintz, J.; Vermilye, H. N.; Leggett, T. H., and Boas, E.: The Effect of Pyloric Obstruction in Relation to Gastric Tetany, *Bull. Johns Hopkins Hosp.* **31**:1-7 (Jan.) 1920. Coller, F. A.; Bartlett, R. M.; Bingham, D. L. C.; Maddock, W. G., and Pedersen, S.: Replacement of Sodium Chloride in Surgical Patients, *Ann. Surg.* **108**:769-782 (Oct.) 1938.

14. McKittrick, L. S., and Sarris, S. P.: Acute Mechanical Obstruction of the Small Bowel: Its Diagnosis and Treatment, *New England J. Med.* **222**:611-622 (April 11) 1940. Calihan and others.<sup>10</sup>

Kennedy and Blain<sup>10</sup> in an attempt to further reduce the attendant mortality in cases of acute mechanical intestinal obstruction. The experiments reported here, in which massive doses of penicillin prolonged the lives of animals with strangulated obstructions to a point which was twice the survival of untreated controls and at which time successful resections were performed, are not intended to encourage delay in operation for acute intestinal obstruction. They are presented, in the first place, as evidence of the great importance of bacterial infection in determination of the outcome of strangulated intestinal obstruction and, in the second place, to demonstrate the value of the preoperative use of massive doses of penicillin in experimental strangulated obstructions.

#### CONCLUSIONS

1. Massive doses of penicillin prolong the lives of experimental animals with strangulated ileal obstructions as compared with untreated controls when in both groups, shock, hemorrhage, chloride and loss of water are combated.
2. After a period twice as long as the survival time of the controls, the strangulated bowel was resected in 5 penicillin-treated dogs, with complete recovery in 4 of these dogs.
3. Therapy with massive doses of penicillin is recommended in all cases of acute intestinal obstruction in which strangulation is believed to be present or in which strangulation cannot be ruled out. This should be an adjunct to and not a substitute for early operation in such obstructions.

## AIR FORCE BATTLE CASUALTIES

An Experience with Acute Injuries of Eight Hundred and Thirty-Nine Battle Casualties from the Eighth Air Force

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AIR FORCE crews in combat are subject to injury not only from enemy gunfire but also from the effects of cold or anoxia at high altitudes, from burns or injury from crash landings or parachute jumps or from a bizarre assortment of accidents within a plane in flight, the commonest of which is being caught in a moving gun turret.

During the course of the year March 1, 1944 to March 1, 1945, 1,054 battle casualties from the Eighth Air Force were admitted to the Sixty-Fifth General Hospital, located at Redgrave Park, Suffolk, England. Two hundred and fifteen of these were admitted as transfers from station hospitals in the vicinity. Eight hundred and thirty-nine were admitted to this hospital for definitive care, directly from their bases, on an average of five and one-half hours after being wounded. The latter group, of 839 patients, forms the basis of this report.

During the course of the year covered by this study there were 6,816 patients admitted to the surgical service, of whom 4,072 were admitted directly from Air Force units. Fifty-four per cent of these Air Force personnel were admitted for surgical diseases, 25 per cent for non-battle-injuries and 20 per cent for battle casualties, the last of which are the subject of this report. The Air Force battle casualties comprised 12.3 per cent of the total patients admitted to the surgical service for the year.

According to Army directives, injuries which occur during the course of a combat mission are classified as battle casualties. Those caused by direct enemy action are designated as battle wounds and those by accident in combat as battle injuries. Of the 839 patients with acute injuries, 645 had battle wounds from missiles, 140 battle injuries from plane crashes, 26 battle injuries from parachute jumps and 28 injuries from plane accidents (table 1).

The patients were members of sixty-six different bomber or fighter groups. The largest number from any one group was 92. Thirteen groups sent over 20 patients each. All casualties except 29 were from heavy bomber groups. The largest number of fresh casualties to arrive

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in any one day was 24. On only nineteen occasions were 10 or more casualties received in any twenty-four hour period.

#### ANALYSIS OF 645 CASUALTIES INJURED BY MISSILES

As shown in table 1, of the acute battle wounds from missiles, five hundred and forty-four were caused by flak, fifty-four by 20 mm. cannon shell, twenty-eight by secondary missiles set in motion usually by flak, fourteen by machine gun shells, three by rifle bullets, one by a rocket and one by bomb fragments. The low proportion of wounds from 20 mm. cannon shell in comparison with those in statistics compiled by the Fifteenth Air Force<sup>1</sup> and by the Eighth Air Force<sup>2</sup> during an

TABLE 1.—*Analysis of Cause of Injury in 839 Battle Casualties*

|  |     |
|--|-----|
| Battle casualties with acute injuries..... | 839 |
| From missiles.....                         | 645 |
| Flak.....                                  | 544 |
| Cannon shell.....                          | 54  |
| Secondary missiles.....                    | 28  |
| Plexiglass.....                            | 25  |
| Plane parts.....                           | 2   |
| Oxygen bottle.....                         | 1   |
| Machine gun shell.....                     | 14  |
| Rifle bullets.....                         | 3   |
| Rocket.....                                | 1   |
| Bomb.....                                  | 1   |
| From crash.....                            | 140 |
| From parachute jump.....                   | 26  |
| From plane accidents.....                  | 28  |
| Caught in turret.....                      | 11  |
| Foot.....                                  | 3   |
| Arm.....                                   | 3   |
| Head.....                                  | 3   |
| Thorax.....                                | 3   |
| Cold injury.....                           | 3   |
| Falls.....                                 | 2   |
| Hit by dropping bombs.....                 | 2   |
| Burns.....                                 | 2   |
| Anoxia.....                                | 1   |
| Struck by prop.....                        | 1   |
| Sprained shoulder throwing chaff.....      | 1   |
| Lung irritation from smoke.....            | 1   |
| Hand injury cleaning gun.....              | 1   |
| Foot injury from floor plate.....          | 1   |
| Hand injury in crank.....                  | 1   |
| Face injury from nose wheel.....           | 1   |

earlier period is explained by the reduction in enemy fighter opposition during the period of this study.

Table 2 shows the location of the eight hundred and sixty-three wounds which occurred in the 645 casualties injured by missiles. Sixty-nine per cent of these wounds occurred in the extremities, 11 per cent in the trunk and 20 per cent in the head and neck. Of the wounds of the extremities fractures occurred in 25 per cent, neural injuries in 8 per cent, and major arterial injuries in 5.5 per cent. Of the wounds

1. Benson, O. O., Jr., and Hoffman, I. L.: A Study of Wounds in Combat Crews, *Air Surgeon's Bull.* 1:1 (July) 1944.

2. MacFee, W. F.: The Treatment of Air Force Combat Casualties, *Ann. Surg.* 120:1 (July) 1944.

of the trunk 40 per cent resulted in visceral penetration. Six additional patients, with wounds of entrance in the neck or extremities, had injuries within the thoracic or the peritoneal cavity.

Table 3 shows the distribution of the 645 men wounded by missiles according to the position of their major injury. The number of cranio-cerebral and thoracic injuries is disproportionately high because patients

TABLE 2.—*Location of the 863 Wounds Occurring in the 645 Patients Injured by Missiles*

| Region                        | Location      | Num-ber | Per Cent | Region                            | Location | Num-ber | Per Cent |
|-------------------------------|---------------|---------|----------|-----------------------------------|----------|---------|----------|
| Head and neck,<br>20 per cent | Head          | 57      | 6.6      | Upper extremity,<br>23.8 per cent | Shoulder | 51      | 5.9      |
|                               | Face          | 52      | 6.0      |                                   | Arm      | 77      | 8.9      |
|                               | Eye           | 44      | 5.1      |                                   | Forearm  | 61      | 7.0      |
|                               | Neck          | 20      | 2.3      |                                   | Hand     | 61      | 7.0      |
| Trunk, 11 per cent            | Thorax        | 43      | 5.0      | Lower extremity,<br>40 per cent   | Thigh    | 170     | 19.7     |
|                               | Abdomen       | 14      | 1.6      |                                   | Leg      | 137     | 15.9     |
|                               | Lumbar region | 6       | 0.6      |                                   | Foot     | 37      | 4.3      |
|                               | Buttock       | 33      | 3.8      |                                   |          |         |          |

with serious injuries of the head and chest from station hospitals in the vicinity, also serving the Air Forces, were sent immediately to this hospital. The low incidence of penetrating thoracic and abdominal wounds as compared with wounds of ground forces in the field<sup>3</sup> is attributed to the effectiveness of body armor worn by crews of heavy bombers in combat. Grow and Lyons<sup>4</sup> have demonstrated a 58 per cent reduction in thoracic wounds and a 36 per cent reduction in abdominal

TABLE 3.—*Distribution of Casualties According to Structures Injured in 645 Fresh Battle Wounds from Missiles*

| Location                    | Cases | Per Cent |
|-----------------------------|-------|----------|
| Soft parts.....             | 373   | 57.8     |
| Skeletal system *.....      | 164   | 25.4     |
| Eye.....                    | 38    | 5.9      |
| Cranio-cerebral region..... | 25    | 3.8      |
| Abdominal region.....       | 18    | 2.8      |
| Faciomaxillary region.....  | 14    | 2.2      |
| Thoracic region.....        | 13    | 2        |

\* Not including head, face or thorax.

wounds in crews of bombers of the Eighth Air Force after the introduction of body armor.

Of 645 airmen wounded by missiles the positions flown by 530 in heavy bombers were recorded. These data are presented in table 4.

3. Hoche, O.: Die wehrchirurgische Behandlung der Verwundeten, Med. Klin. 35:1532, 1939; Bull. War Med. 1:1 (Sept.) 1940.

4. Grow, M. C., and Lyons, R. C.: Body Armor: A Brief Study of the Development. Air Surgeon's Bull. 2:8 (Jan.) 1945.



TABLE 4.—Analysis of Injuries in Crews of Heavy Bombers According to their Position in Plane

| Position in plane.....     | Pilot   |    | Co-pilot |    | Navigator |    | Bombardier |    | Radio Man |    | Ball Turret Gunner |    | Top Turret Gunner |    | Waist Gunner (2) |     | Tail Gunner |    |
|----------------------------|---------|----|----------|----|-----------|----|------------|----|-----------|----|--------------------|----|-------------------|----|------------------|-----|-------------|----|
| Number of men injured..... | 37      | 48 | 29       | 31 | 69        | 52 | 51         | 45 | 50        | 65 | 12                 | 50 | 33                | 40 | 135              | 182 | 90          | 32 |
| Total wounds.....          | Num-ber |    | Per Cent |    | Num-ber   |    | Per Cent   |    | Num-ber   |    | Per Cent           |    | Num-ber           |    | Per Cent         |     | Num-ber     |    |
| Location of Wounds         |         |    |          |    |           |    |            |    |           |    |                    |    |                   |    |                  |     |             |    |
| Head.....                  | 3       |    | 1        |    | 3         |    | 6          |    | 7         |    | 1                  |    | 2                 |    | 15               |     | 5           |    |
| Face.....                  | 7       | 23 | 2        |    | 9         |    | 7          |    | 6         |    | 1                  |    | 1                 |    | 9                |     | 1           |    |
| Eye.....                   | 1       |    | 2        | 12 | 1         | 25 | 10         | 21 | 1         |    | 5                  | 11 | 1                 | 17 | 9                | 19  | 3           | 16 |
| Neck.....                  | 3       |    | 0        |    | 1         |    | 5          |    | 0         |    | 0                  |    | 3                 |    | 3                |     | 1           |    |
| Shoulder.....              | 2       |    | 3        |    | 7         |    | 7          |    | 3         |    | 2                  |    | 1                 |    | 11               |     | 4           |    |
| Arm.....                   | 7       |    | 3        |    | 5         |    | 11         |    | 5         |    | 5                  |    | 1                 |    | 21               |     | 6           |    |
| Forearm.....               | 2       | 31 | 9        | 30 | 11        | 29 | 10         | 35 | 6         | 25 | 2                  | 32 | 0                 | 27 | 6                | 27  | 7           | 29 |
| Hand.....                  | 4       |    | 1        |    | 10        |    | 11         |    | 3         |    | 2                  |    | 1                 |    | 9                |     | 7           |    |
| Chest.....                 | 2       |    | 4        |    | 7         |    | 8          |    | 6         |    | 2                  |    | 1                 |    | 5                |     | 1           |    |
| Abdomen.....               | 0       |    | 1        |    | 2         |    | 0          |    | 0         |    | 1                  |    | 9                 |    | 5                |     | 2           |    |
| Lumbar region.....         | 0       |    | 0        | 15 | 1         | 15 | 1          | 9  | 2         | 15 | 0                  | 10 | 0                 | 5  | 3                | 12  | 1           | 12 |
| Buttock.....               | 0       |    | 0        |    | 1         |    | 2          |    | 2         |    | 2                  |    | 1                 |    | 11               |     | 6           |    |
| Thigh.....                 | 10      |    | 7        |    | 11        |    | 15         |    | 11        |    | 15                 |    | 11                |    | 16               |     | 18          |    |
| Leg.....                   | 6       | 35 | 4        | 42 | 9         | 24 | 18         | 31 | 9         | 10 | 51                 | 10 | 53                | 22 | 41               | 15  | 15          | 42 |
| Foot.....                  | 1       |    | 3        |    | 1         |    | 1          |    | 1         |    | 2                  |    | 1                 |    | 6                |     | 2           |    |

The incidence of injuries in pilots, co-pilots and turret gunners was somewhat lower than in those flying other positions. The table does not show any significant difference in the location of wounds according to the position flown in the plane.

Treatment of injured air force casualties was begun by the crew in the plane before it landed. The presence of mind of these men and their efficiency in caring for fellow crew members spoke well for their training and equipment. The readjustment of oxygen masks and oxygen supply, application of pressure bandages to control hemorrhage, closure of sucking wounds of the chest by appropriate dressings, relief of pain by morphine and application of warmth were all done effectively by these men working under the adverse conditions of flight at high altitude.

When the aircraft landed at its base a wounded man was first seen by his flight surgeon. If he were seriously wounded or had a fracture of a long bone, his removal from the plane was often difficult. It was accomplished with greatest ease and least harm to the patient by first wrapping him in a Neil Robertson litter (fig. 1). He then usually remained in this litter until he was put on the operating table at the hospital.

From the plane an injured airman was first taken to the medical station on the field where he landed. Here the first aid measures begun on the plane were checked and continued, and plasma was given if necessary to restore blood pressure. Prolonged efforts to combat shock were not advisable at the base, and, after several bottles of plasma had been given, if the condition was not much improved the administration of plasma was continued in the ambulance and the patient brought on to the hospital.

*Resuscitation and Triage.*—At the hospital, casualties were received in the shock ward, where they were placed on a bed without first being removed from the stretcher or Neil Robertson litter. Those with wounds of the head or chest were placed with the head of the bed elevated 8 inches (20 cm.). Others were placed with the head lowered a similar distance. In the shock ward the blood pressure and pulse were taken, general condition appraised, shock combated, clothes removed (usually by cutting them off), wounds inspected and a rapid but complete examination done, particular attention being paid to possible injuries of nerves, bones, tendons or blood vessels in wounds of extremities and to the possibility of thoracic or abdominal penetration in all wounds over the trunk, shoulders, neck, buttocks or upper part of the thighs. A history of the injury and description of the physical findings was recorded, roentgenograms of the affected part taken, preoperative medication given (usually 1 cc. of tetanus toxoid and 0.6 mg. of atropine) and the skin surrounding the wound shaved. This was done, more or less in the order as given, prior to removal to the operating room.

Roentgenograms of all casualties were taken before operation. My colleagues and I have seen a patient in whom a piece of flak entered the shoulder below the level of the insertion of the deltoid and lodged in the lower lobe of a lung. In another patient the missile entered the lateral surface of the thigh at the junction of the middle and lower third and lodged in the bladder. Frequently missiles entering the buttock penetrated the peritoneal cavity or injured the rectum below the pelvic floor. For this reason roentgenograms of a large area of the body, including anteroposterior, lateral and often oblique views, were necessary if the true nature of the wound were to be recognized.

Shock was treated with transfusions of whole blood. While plasma was undoubtedly of great value in the first aid treatment of shock, it

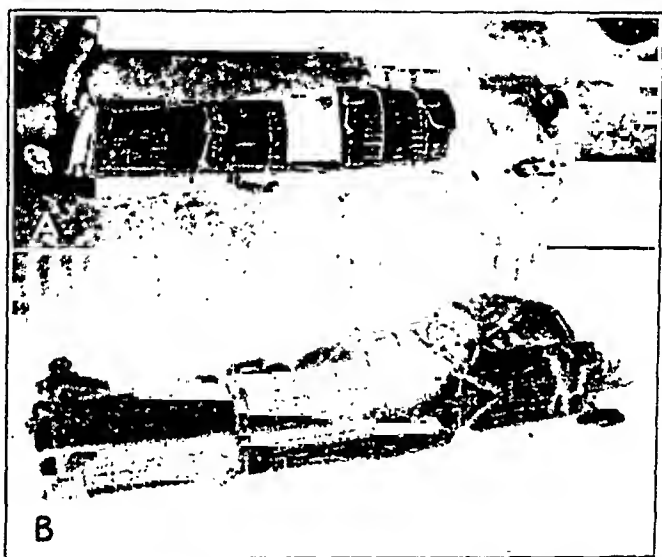


Fig. 1.—*A*, the Neil Robertson litter, used in removing casualties from the plane and in transporting them to the hospital. *B*, another view of the Neil Robertson litter, showing its under surface.

had little place in its management in the hospital. Large transfusions were often necessary, and we have frequently given 8 or 10 bottles of blood before and during operation. This blood was supplied through our own blood bank, from donors in our detachment and from the air fields.

Warmth was supplied only by the application of blankets. Oxygen was available at all beds in the shock ward. It was given to the patients with thoracic injuries and occasionally to those in shock. Adrenal cortex extract has not been used. Morphine had usually been given by crew members or at the base, and further administration was rarely necessary.

The copper sulfate method of estimating values for specific gravity of blood and plasma was employed. From these figures the estimation

of hemoglobin, hematocrit and plasma protein levels was calculated, and the results were used in determining the therapy for most of the patients with shocking injuries. The procedure was of most value in following the hemoconcentration of burns. In a patient who had suffered a traumatizing injury with loss of blood and had in addition received plasma at his base before being brought to the hospital, the information which it supplied was often not of great value. We preferred to estimate the degree of shock from a general clinical appraisal of the condition rather than from any one laboratory aid.

If concealed hemorrhages were suspected, we did not hesitate to begin operation on any patient as soon as he had received rapidly several bottles of blood and had an intravenous cannula in place, with blood running into the vein smoothly. In all others we preferred to wait until recovery from shock had begun. The administration of blood was continued during operation in all patients who had been in shock or in whom the development of shock was anticipated.

Reactions to transfusions had to be guarded against. The use of transfusions of 2, 3 or 4 liters of blood to combat shock and to help sustain a patient through the prolonged and oftentimes traumatizing operation necessary to repair the damage of war injuries has been one of the major developments in the surgical therapy of this war. However, hemolytic reactions to transfusions are probably more prone to follow these large, multiple or repeated transfusions. Hemoglobinuric nephrosis with uremia was the cause of death in 1 of the 3 patients dying from missile wounds in this series. It also developed following transfusion in 2 injured men before they were transferred to us from station hospitals. They are not included in this series of acute injuries in battle casualties. In an airman with a third degree burn of 65 per cent of his body surface, incurred after a crash landing, a similar condition was found at autopsy.

Alkalinization of the urine was carried out in an endeavor to prevent the renal damage resulting from hemoglobinemia and hemoglobinuria. In cases of elective transfusions this was routinely carried out by the giving of sodium bicarbonate or sodium citrate by mouth before the transfusion was given. In cases requiring large transfusions as an emergency measure, an additional 1.25 Gm. of sodium citrate intravenously was given with each bottle of blood and, if a reaction occurred, at two hour intervals until the urine was alkaline or was free of hemoglobin.

Wounds of the soft parts, not including visceral penetrations, accounted for 373, or 57 per cent, of the patients with battle wounds from missiles. These wounds were treated by excising all devitalized tissue, removing foreign bodies, irrigating with isotonic solution of sodium chloride, dusting lightly with sulfanilamide powder in most of

the cases (average 5 Gm. per patient), inserting loosely a gauze strip covered well with petrolatum to the depth of the wound and applying a voluminous dressing snugly. Forceful packing of a wound was not done. Ample incisions through skin and fascia along the natural lines of skin cleavage are necessary for adequate exposure. Transverse incisions in the extremities are not advised.

The extent of the débridement was dependent on the nature of the wound. In some wounds, where the missile struck at high velocity, a wide excision of traumatized tissue was necessary. In others, caused by missiles of low velocity, little damage was done and a minimal excision of the entire wound was necessary. Usually the débridement had to be done in layers as the various tissue planes presented. Only rarely was en bloc excision of the entire wound possible. Most wounds had portions of woolen flying suit along the tract, and often wool was wrapped around the missile. For this reason effort was made to remove all foreign bodies. This was usually not difficult, as the wound tract could be followed to the missile. Small fragments of shells often could not be easily located, and, if in a position where their presence would cause no harm, no prolonged search was made for them.

Sulfanilamide crystals were lightly dusted into the wounds of about 80 per cent of the patients. Except for an increased discharge of tissue fluid and blood from the wounds, no harm was noted from its local use in wounds left open for later secondary suture. In the group of patients in whom it was not used there was no essential gross difference in healing of wounds from the healing in treated patients.

Sulfadiazine was given routinely by mouth until after secondary closure of the wound had been done. When penicillin became readily available it was given in doses of 20,000 units every three hours for four or five days to patients with major wounds. Pentothal sodium was the anesthetic agent used in most cases, although some débridements were done under regional block or direct infiltration of procaine hydrochloride.

Wounds in the scalp, face and all serous cavities were closed after excision. All others were left open and not dressed until five days later, when the patient was returned to the operating room, dressings and petrolatum gauze removed and secondary closure done. If secondary closure was impossible because of the size of the wound, grafting with split thickness skin grafts was done at the time (figs. 2, 3 and 4).

Wounds of the skeletal system, not including ribs or bones of the face or skull, were present in 164, or 25 per cent, of the patients with battle wounds from missiles (table 3). Bones involved are shown in table 5. In their care the wounds of the soft parts were débrided as described. All loose fragments of bone were removed. The wounds were then irrigated with isotonic solution of sodium chloride and lightly dusted with sulfanilamide, and petrolatum gauze was inserted loosely.



Fig. 2.—*A*, a gutter wound of the right thigh and a perforating wound of the left thigh from flak as seen on admission. *B*, the wounds after secondary closure and grafting, five days later. *C*, complete healing after fourteen days.

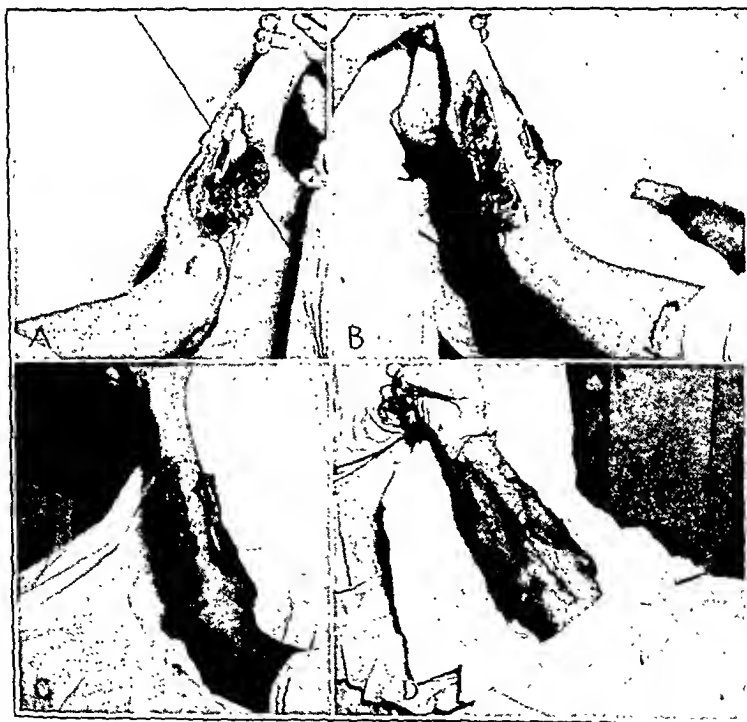


Fig. 3.—*A*, a perforating wound from flak through the leg as seen on admission. *B*, patient viewed from the opposite side. *C*, wounds on removal of dressings, five days after débridement. *D*, wounds after application of split thickness grafts on the same day.

In cases of injuries of the long bones requiring traction to maintain bone length, skeletal traction was then applied. In all others and in



Fig. 4.—Same patient as in figure 3, showing complete healing.

TABLE 5.—*Bones Involved in 164 Cases of Wounds from Missiles with Skeletal Injury*

| Location                     | Number | Bones                 |
|------------------------------|--------|-----------------------|
| Long bones.....              | 3      | Radius and ulna       |
|                              | 6      | Radius alone          |
|                              | 15     | Ulna                  |
|                              | 23     | Humerus               |
|                              | 22     | Femur                 |
|                              | 4      | Tibia and fibula      |
|                              | 18     | Tibia alone           |
|                              | 16     | Fibula alone          |
|                              | 11     | Phalanges of the hand |
|                              | 12     | Metacarpals           |
| Hands and feet.....          | 6      | Carpals               |
|                              | 8      | Tarsals               |
|                              | 5      | Metatarsals           |
|                              | 5      | Scapula               |
| Miscellaneous.....           | 6      | Pelvis                |
|                              | 3      | Patella               |
|                              | 2      | Vertebra              |
|                              | 2      | Elbow joint           |
|                              | 2      | Knee joint            |
|                              | 3      | Thigh                 |
| Amputations (Immediate)..... | 4      | Leg                   |
|                              | 1      | Foot                  |
|                              | 4      | Toes                  |
|                              | 2      | Fingers               |

injuries of the long bones, where damage to muscle was so extensive or loss of bone so pronounced that traction was not necessary, well padded plaster casts were applied. Shattering of bone was often exten-

sive (fig. 5). Internal or external skeletal fixation was not used. The first dressings were done in the operating room five days after débridement, at which time the wounds were closed if possible by suture or skin graft.

Wounds penetrating the skull or brain occurred in 25, or 3.8 per cent, of the 645 casualties injured by missiles. Sixteen of these were penetrating wounds of the skull and brain, usually with indriven fragments of bone, while 9 resulted in fractures of the skull, usually depressed, without dural penetration. In all cases the scalp was débrided, loose fragments of skull removed, the defect of the skull enlarged, traumatized



Fig. 5.—Roentgenogram of a leg after a wound from flak, showing the typical comminution of a bone which occurs when it is struck by missiles of high velocity.

brain removed by suction and especial care taken to remove indriven fragments of bone. Bleeding was painstakingly controlled by coagulation or with silver clips and, in cases of venous sinus tears, by muscle packs or fibrin foam. In cases of penetrating wounds, dural grafts from temporal fascia, periosteum or fascia lata were usually necessary. If the defect of the bone was not repaired with a tantalum plate immediately, tantalum foil was usually placed between the scalp and dura to make subsequent plating easier. The wounds of the scalp were always closed.

Of these 25 patients, 1 with an extensive penetrating craniofacial wound from a 20 mm. cannon shell died (mortality 4 per cent). All the others made good recoveries. All except 1 were ambulant on dis-



charge. Four patients returned to duty. The others were returned to the United States.

Thoracic injuries occurred in 13, or 2 per cent, of the patients wounded from missiles. In none of these patients did the missile traverse the flak suit. In 1 the suit was not worn. In 1 the missile entered under the suit. In 5 the penetration occurred in the lateral unprotected portion of the chest, between the anterior and posterior axillary lines. In 4 the missiles entered through the shoulder and in 2 through the neck (fig. 6). We are convinced that the body armor



Fig. 6.—Four casualties with flak wounds of the chest, showing typical sites of penetration through shoulder, neck or lateral surface of the thorax. The chest is protected anteriorly and posteriorly by body armor worn by air force crews in combat.

worn by crew members of heavy bombers has greatly reduced the incidence of thoracic wounds.

Penetrating wounds occurred eight times, the missiles lodging in the lung in 4 patients, in the mediastinum in 2 and in the opposite thoracic wall in 2. In 2 patients the missile traversed the lung and both walls of the thorax, in 1 of these patients also going through the dome of the diaphragm and the right lobe of the liver. Tangential sucking wounds with shattered ribs but without penetration of the lung occurred in 3 cases.

Thoracotomy with the patients under ether administered endotracheally as soon as they could be prepared for operation was done in all except 1 case in which a tiny fragment from a 20 mm. cannon shell had lodged in the lung and no operation was necessary. The missiles were removed in all the other cases.

The thorax was opened through the wound of entry in all cases except those in which the missile entered through the apex, in which cases an anterior approach through the third interspace was used. The wounds of the soft parts of the chest were débrided, the shattered rib fragments removed, particular care being paid to the removal of fragments driven into the lung or pleural cavity, the foreign body removed, the wound in the lung closed with sutures, the blood removed from the pleural cavity and the wounds of the soft part of the chest, exclusive of skin and subcutaneous tissue, closed without drainage. At the close of the procedure air was removed from the pleural cavity with a catheter or needle and 100,000 units of penicillin introduced. Thereafter daily thoracentesis was done until the chest was dry and the lung reexpanded.

There were no deaths in this series of patients with thoracic injuries. Empyema developed in 1 patient and was treated by drainage by catheter and rib resection. In 1 patient, with perforation of two lobes of the lung, reexpansion of the lung was not complete when the patient was evacuated to the United States. In another, in whom ligation of the subclavian artery just above the aorta was necessary, a partial clotted hemothorax was present when the patient was evacuated. Decorication was not done because of the development of jaundice in this patient. In all other patients complete restoration of function occurred in the damaged lungs.

Abdominal injuries requiring laparotomy occurred in 18, or 2.8 per cent, of the patients injured by missiles. The viscera damaged are shown in table 6. Ether administered endotracheally was the anesthetic used in each case. Perforations of the stomach and small intestine (fig. 7) were closed. In 1 case four complete end to end anastomoses were necessary in the small intestine. In colonic injuries the colon was extraperitonealized as a colostomy. Splenectomy was done for the one ruptured spleen. Cholecystectomy was performed for the perforated gallbladder. The pancreatic wound was drained, and the resultant pancreatic fistula closed spontaneously in a month. The wounds of the bladder were closed about a suprapubic catheter. A loop colostomy and perineal drainage of the perirectal tissues were done for the penetrating wound of the sacrum with perforation of the extraperitoneal portion of the rectum. Exploratory laparotomy and suprapubic cystotomy were done for the perineal wound with laceration of the urethra.

Two of these 18 patients died (mortality 11 per cent). One, in whom a large shell fragment had traversed the iliac bone, small intestine

and colon, died in twenty-four hours, with high temperature, stupor and hemiplegia from fat embolism of the brain. Another, with compound fractures of the humerus and femur and a penetrating abdominal wound with perforation of the gallbladder, in whom repeated blood transfusions were necessary, died eighteen days later, in uremia. The kidneys



Fig. 7.—A penetrating abdominal wound in the left flank, with evisceration of small intestine. There were numerous perforations of the descending colon and small intestine and one of the bladder. The missile lodged in the right thigh. The wound of entrance is in a part of the abdomen unprotected by the flak suit.

showed the typical changes of hemoglobinuric nephrosis. All other patients made good recoveries. All colostomies were closed. Eight patients were returned to duty and 7 evacuated to the United States.

Injuries to the eyes occurred in 38 patients as the primary cause for admission. In 6 others injuries of the eyes occurred as incidental

TABLE 6.—*Location of Wounds in 18 Cases Requiring Laparotomy Following Injury by Missiles*

| Number | Location                                 |
|--------|--|
| 3      | Retroperitoneal hematoma                 |
| 2      | Herniated omentum                        |
| 2      | Small intestine (multiple)               |
| 2      | Small intestine and colon (multiple)     |
| 1      | Small intestine, colon and bladder       |
| 1      | Gallbladder, liver, pancreas and stomach |
| 1      | Stomach and liver                        |
| 1      | Liver                                    |
| 1      | Bladder                                  |
| 1      | Spleen                                   |
| 1      | Gallbladder                              |
| 1      | Rectum and ureter                        |
| 1      | Urethra                                  |

findings. There were intraocular foreign bodies in sixteen instances, foreign bodies in the cornea or conjunctiva in sixteen, rupture of the globe in three, lacerations of the cornea in eleven and intraocular hemorrhage in two. Six enucleations were necessary. Intraocular foreign bodies were removed in 8 cases.

Faciomaxillary injuries occurred in 14 cases. The maxilla was penetrated eight times and the nose twice, and in seven instances the

mandible was fractured. Wounds of the soft parts were débrided, with care not to sacrifice skin of the face unnecessarily. Wounds were then closed by primary suture. Fractures of the mandible were reduced and immobilized by intramaxillary multiple loop wiring with intermaxillary elastics for fixation by members of the dental service. Penetrating wounds of the maxilla were usually drained through a nasoastral window after débridement of bone fragments.

In 1 case a shell fragment penetrated the neck and pierced the hypopharynx. It was removed on laryngoscopic examination from the interarytenoid fold. The wound in the neck was explored, the injury to the hypopharynx débrided and closed and a tracheotomy done. The tracheotomy tube was removed in four days and the secondary closure done on the wound of the neck on the fifth day. Recovery was uneventful.

Injuries to the peripheral nerves occurred in 48 patients. The distribution of these cases is shown in table 7. Because of difficulty in

TABLE 7.—*Nerves Injured in 645 Battle Casualties Wounded by Missiles*

Immediate amputation was done in the case of the median and ulnar lesion and 3 cases of sciatic lesions.

| Number | Nerve            | Number | Nerve    |
|--------|------------------|--------|----------|
| 1      | Brachial plexus  | 9      | Sciatic  |
| 1      | Median and ulnar | 6      | Tibial   |
| 6      | Median           | 3      | Peroneal |
| 9      | Ulnar            | 1      | Facial   |
| 9      | Radial           | 1      | Digital  |
| 1      | Axillary         | 1      | Plantar  |

detecting how widely a divided nerve is traumatized by shell fragments at the time of the original excision of the wound, nerve suture was rarely done until three weeks after the wound had been closed by secondary suture or graft. At this time the tantalum wire suture technic with tantalum foil cuff, as introduced by Col. R. Glenn Spurling, was used.

Arterial injuries occurred in 35 patients with injury due to missiles (table 8). In all cases bleeding had stopped by the time the patients arrived at the hospital, either because of arterial spasm, intravascular thrombosis or the presence of retained extravascular clots or because of a combination of these factors. Loss of blood had been severe in some, and transfusions were necessary in most of the cases. Direct visualization of the damaged artery with adequate exposure was necessary for proper management of the vessel without damage to the adjacent nerves. Temporary control of the bleeding artery was obtained by tourniquet or direct digital pressure on the bleeding vessel or by a tape placed about the artery above the injury. Vessels were ligated with either surgical gut or silk and were transfixed. Ligation in con-

tinuity of an artery was not done. The accompanying vein was ligated whenever a major artery was tied off.

Immediate amputation was done in three of the femoral, two of the popliteal and one of the radial and ulnar lesions, because of extensive injuries to the extremity. Gangrene of the foot subsequently developed in the external iliac lesion and of the foot and leg in one of the femoral and the remaining three popliteal injuries, necessitating amputation. Of these delayed amputations gas gangrene developed in the femoral and one of the popliteal injuries and hastened the removal of the leg.

Arterial suture was done five times, once in the common carotid artery, twice in the popliteal artery, once in the femoral artery, at the level of the entrance of the artery into the adductor canal, and once in a radial artery, where it was necessary to ligate the ulnar artery. Heparin was not available in any of the cases. Thrombosis occurred at the site of both popliteal sutures, collateral circulation was not sufficient to maintain the life of the extremity and amputation was neces-

TABLE 8.—*Major Arteries Involved in 645 Casualties Injured by Missiles*

Immediate amputation was necessary in 3 cases of femoral, 2 of popliteal and 1 of radial and ulnar lesions because of extensive injury to the extremities.

| Number | Artery                   | Number | Artery            |
|--------|--------------------------|--------|-------------------|
| 1      | Common carotid           | 1      | External iliac    |
| 1      | Internal maxillary       | 6      | Femoral           |
| 1      | Costocervical trunk      | 2      | Profundus femoral |
| 1      | Subclavian (mediastinal) | 5      | Popliteal         |
| 2      | Brachial (upper third)   | 9      | Posterior tibial  |
| 1      | Brachial (at elbow)      | 3      | Peroneal          |
| 2      | Radial and ulnar         |        |                   |

sary. Adequate circulation was maintained after the other arterial sutures.

Secondary hemorrhage or the development of an aneurysm did not occur in any of these cases. In 1 case an unrecognized injury to a posterior tibial artery resulted in an aneurysm, which was later excised. In another case, in which an injury to the posterior tibial artery was recognized and the vessel ligated, secondary hemorrhage occurred on the twelfth day from an injured peroneal artery which was not recognized at the time of the original débridement. The bleeding peroneal artery was located and ligated without disturbing the viability of the limb.

*Bacterial Flora.*—Débrided tissue was cultured in 177 cases. Organisms of the Clostridium group were present in 73, or 41.2 per cent, of the cases. Of these *Cl. welchii* was present thirty-eight times, *Cl. oedematiens* eleven, *Cl. septicum* eighteen, *Cl. sporogenes* nine, *Cl. histolyticum* nine, *Cl. tertium* four and *Cl. tetanomorphum*, *Cl. tetani* and *Cl. fallax* once each. *Staphylococcus aureus* was present one hundred and fifty-four times, in forty-seven of which the organisms were hemo-

lytic. Streptococci were present in 98 cases. In 14 of these the organisms were hemolytic and in 39 anaerobic. Organisms of the coliform group were present in only 4 cases.<sup>5</sup> This bacteriologic flora is essentially the same as that found in civilian wounds by Altemeier and Gibbs.<sup>6</sup>

Infection with *Cl. welchii* occurred in 2 patients. In a femoral and in the other a popliteal artery had been ligated at the time of débridement. Amputation was necessary in both cases.

In none of the wounds of the other patients in this series did cellulitis develop or was infection present grossly in the wound at the time of secondary closure. In one scalp wound and one thoracic wound, both closed at the time of the original operation, localized infections developed, which were drained.

Secondary closures were almost uniformly successful, and in the small number (estimated at 5 per cent) in which healing was not complete and drainage occurred lack of success was attributed to tension on the sutures or to the presence of dead space in the wound rather than to the presence of infection.

*Mortality*—Death occurred in 3 of the 645 patients injured by missiles (mortality 0.4 per cent). In 1, death was from an extensive craniocerebral wound from a 20 mm. cannon shell. The other 2 had abdominal wounds, 1 dying of fat embolism in twenty-four hours and the other of uremia from hemoglobinuric nephrosis after eighteen days. These patients are discussed more fully under the paragraphs on abdominal and craniocerebral wounds.

Return to duty was possible for 439, or 68 per cent, of the patients. Two hundred and three were sent to the United States.

#### ANALYSIS OF 140 CASUALTIES INJURED IN CRASHES

One hundred and forty of the 839 battle casualties (table 1) occurred as a result of crashes during combat missions. The sites of these injuries are shown in table 9. Most of the injuries were multiple.

Injuries of the head occurred most frequently. They were present in 65, or 46 per cent, of the casualties wounded in crashes. Of these, 18 had compound fractures of the skull, all with severe injury to the brain. Eight of the fractures were depressed. Twenty-two other patients had wounds of the scalp with cerebral concussion or contusion without demonstrated fractures of the skull.

Crushing injuries to the vertebrae were the next commonest lesion. Twenty-three patients had vertebral injuries, most of which were multiple. Two had complete lesions of the spinal cord. Only 1 injury,

5. Schuyler, L. H.: To be published.

6. Altemeier, W. A., and Gibbs, E. W.: Bacterial Flora of Fresh Accidental Wounds, Surg., Gynec. & Obst. **78**:164 (Feb.) 1944.

occurred in the cervical portion of the spine. All the others were in the lower six thoracic and upper four lumbar vertebrae.

Burns occurred in 14 patients. These usually involved only the face, head and neck, although 1 casualty had third degree burns over 65 per cent of his body surface.

Fifteen of the 140 patients injured in crashes died (mortality 10.7 per cent). Twelve of these died within the first twenty-four hours. All had multiple injuries and were in desperate condition when admitted. In 11 of these the immediate cause of death was thought to be an

TABLE 9.—*Site of Injury in 140 Patients Injured in Plane Crashes*

| Location                                       | Number | Injury                          |
|--|--------|---------------------------------|
| Head.....                                      | 25     | Injury of scalp                 |
|  | 18     | Injury of craniocerebral region |
|  | 22     | Injury of scalp and concussion  |
| Faciomaxillary region.....                     | 4      | Injury of mandible              |
|  | 2      | Injury of maxilla               |
|  | 2      | Injury of nose                  |
| Abdomen.....                                   | 1      | Injury of gallbladder           |
| Thoracic area.....                             | 12     | Injury of ribs (multiple)       |
| Regions requiring treatment by plastic surgery | 14     | Burns                           |
| Soft parts.....                                | 15     | Contusions; sprains             |
| Shoulder.....                                  | 1      | Dislocation                     |
| Acromioclavicular area.....                    | 2      | Dislocation                     |
| Hip.....                                       | 4      | Dislocation                     |
| Elbow.....                                     | 1      | Dislocation                     |
| Forearm.....                                   | 1      | Amputation                      |
| Leg.....                                       | 1      | Leg                             |
| Fingers.....                                   | 2      | Fingers                         |
| Long bones.....                                | 1      | Fracture of radius and ulna     |
|  | 1      | Fracture of shaft of radius     |
|  | 1      | Fracture of head of radius      |
|  | 2      | Fracture of ulna                |
|  | 6      | Fracture of humerus             |
|  | 10     | Fracture of femur               |
|  | 14     | Fracture of tibia and fibula    |
|  | 4      | Fracture of tibia               |
| Miscellaneous sites.....                       | 23     | Fracture of vertebra            |
|  | 6      | Fracture of pelvis              |
|  | 3      | Fracture of clavicle            |
|  | 1      | Fracture of scapula             |
|  | 6      | Fracture of ankle               |
|  | 2      | Fracture of tarsal              |
|  | 3      | Fracture of metatarsal          |
|  | 3      | Fracture of carpal              |
|  | 3      | Fracture of metacarpal          |

injury of the head, while in the twelfth a crushing injury of the chest was the principal cause of death.

One patient, with a fracture dislocation of the fifth and sixth cervical vertebrae and quadriplegia, died on the third day. Another, with a compound depressed fracture of the skull through the frontal and ethmoid sinuses died of meningitis, on the eighth day. Two of the burned patients died, 1 with burns of the face, head and hands of asphyxia from edema of the larynx on the second day and the other with severe burns of 65 per cent of the body surface from toxemia and renal suppression on the fourth day. Microscopic changes of hemoglobinuric nephrosis were found in the kidneys of the last patient. The death from asphyxia was so sudden that it could not be relieved even though

a tracheotomy set was at hand and the possibility of a laryngeal obstruction had been foreseen. It could have been prevented had a prophylactic tracheotomy been done immediately on the man's admission to the hospital. This procedure was subsequently carried out on all with severe burns of the head in whom the possibility of the inhalation of flames was present.

Sixty-five, or 46 per cent, of the casualties injured in crashes were returned to duty. Sixty were returned to the United States.

#### ANALYSIS OF 26 CASUALTIES INJURED IN PARACHUTE JUMPS

Twenty-six men were injured in parachute jumps from disabled planes during combat missions and were hospitalized immediately. The sites of the twenty-eight injuries incurred in these 26 men are shown in table 10. All the fractures were simple ones. Sixteen men were returned to duty, and 10 were sent to the United States. None died.

TABLE 10.—*Site of Injury in 26 Patients Injured in Parachute Jumps*

| Location                                       | Number | Injuries                          |
|--|--------|-----------------------------------|
| Long bones.....                                | 2      | Fracture of humerus               |
|  | 2      | Fracture of tibia and fibula      |
|  | 4      | Fracture of ankle                 |
| Miscellaneous sites.....                       | 1      | Fracture of pelvis                |
|  | 3      | Fracture of first lumbar vertebra |
|  | 1      | Fracture of metatarsal            |
| Head.....                                      | 3      | Concussion                        |
| Faciomaxillary region.....                     | 1      | Maxilla                           |
| Regions requiring treatment by plastic surgery | 2      | Burns                             |
| Ankle.....                                     | 3      | Sprain                            |
| Foot.....                                      | 1      | Sprain                            |
| Back.....                                      | 5      | Sprain                            |

#### ANALYSIS OF 28 CASUALTIES RESULTING FROM PLANE ACCIDENTS

Table 1 gives an analysis of the types of accidents occurring in a plane during combat for which hospitalization was necessary. Eleven of these injuries occurred when some part of the body was caught in a moving turret. The top turret was involved in seven and the ball turret in four of these accidents. Only 3 patients were admitted for cold injury during the year of this study. This low figure is evidence of the improvement in equipment and plane design over the earlier years of the war.

Two fatalities occurred in this group. Both of the patients were tail gunners, who suffered severe injuries of the head when struck by an unexploded bomb dropped from above. Both died shortly after admission. All other patients were returned to duty except 1 in whom contusion of the radial, median and ulnar nerves from an injury by a turret necessitated return to the United States.



## SUMMARY

Sixty-nine per cent of wounds from missiles received by Air Force crews in combat occur in the extremities, 11 per cent in the trunk and 20 per cent in the head and neck. Of wounds of the extremities 25 per cent result in compound fractures, 8 per cent in neural injury and 5.5 per cent in major arterial injury.

Body armor worn by the crews of heavy bombers in combat has reduced the number of penetrating thoracic and abdominal wounds.

Injuries of the head and back occurred most frequently after plane crashes and injuries of the back and ankle after parachute jumps. The commonest accident within a plane in flight is the wedging of some part of the body in a moving turret.

The bacterial flora from débrided tissues of Air Force casualties is not unlike that reported from civilian wounds occurring on the ground. The high incidence of organisms of the *Clostridium* group (41.2 per cent) is attributed to the presence of wool from flying suits, which was present in most of the wounds.

The low incidence of infection in wounds is attributed to the fact that adequate surgical treatment was available on an average of five and one-half hours after wounding. The use of the sulfonamide drugs and penicillin presumably contributed to the low rate of infection; however, these agents were considered to be subordinate to adequate wound débridement.

The low mortality in wounds from missiles (0.4 per cent) is attributed to skilful first aid administered in the plane and on the landing fields, to adequate surgical treatment made possible by plasma, to multiple transfusions and anesthetic administered endotracheally and to the control of infection by operation and chemotherapy. Of all these factors the use of transfusions of whole blood, which have made adequate surgical treatment possible, has contributed the most to the low mortality.

## ORBICULARIS ORIS MUSCLE IN DOUBLE HARELIP

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**D**URING operations on 3 patients with double harelip, a modification of one of the usual plastic procedures was evolved.<sup>1</sup> The essential feature of this change was to join the sphincter muscles of each side across the premaxilla, and, to this end, it was necessary to cut deeply into the lip at right angles to its edge in order that a flap of sufficient length could be sewn to the corresponding structure of the opposite side. What was not known at the time was how much sphincter oris muscle was present. It is the purpose of this article to give the anatomy of this muscle in double harelip.

The structure of the orbicularis oris muscle in the lower lip is of little concern in this report. Nor is there much to say about the lip portion of the premaxilla except to record in agreement with Ritchie,<sup>2</sup> Veau and Plessier,<sup>3</sup> Boyd,<sup>4</sup> Peyton<sup>5</sup> and Mullen<sup>6</sup> that it has no striated muscle.

The orbicularis oris muscle is an unusual muscle not only in that its origin is in muscle but also in that some of its insertion, besides that to the skin and mucous membrane, is also in muscle. It is built around the buccinator muscle, which divides as it approaches the corner of the mouth. The middle portion of the buccinator muscle has its origin in the pterygomandibular raphe, and its fibers decussate, the superior division going along the upper portion of the lower lip and the inferior division extending along the lower portion of the upper lip. In either case the fibers meet the ones from the opposite side and, in addition, attach themselves to a less extent to the skin and least to

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From the departments of anatomy and surgery of the Johns Hopkins University School of Medicine.

1. Lee, F. C.: Underlying Principles in the Repair of Double Harelip, *J. M. A. Georgia* **23**:383, 1934.

2. Ritchie, H. P.: Congenital Cleft Lip and Palate, *Ann. Surg.* **84**:211, 1926.

3. Veau, V., and Plessier, P.: Traitement du bec-de-lièvre bilatéral total, *J. de chir.* **40**:321, 1932.

4. Boyd, J. D.: The Classification of the Upper Lip in Mammals, *J. Anat.* **67**:409, 1933.

5. Peyton, W. T.: The Dimensions and Growth of the Palate in Normal Infant and in Infant with Gross Maldevelopment of the Upper Lip and Palate, *Arch. Surg.* **22**:704 (May) 1931.

6. Mullen, T. F.: Congenital Cleft Lip, *M. J. & Rec. (supp.)* **122**:402, 1925.

the mucous membrane in the general region of the midline. The uppermost fibers of the buccinator muscle, having their origin primarily in the maxilla, pass directly forward across the upper lip; the lowermost fibers, arising chiefly from the mandible, extend directly forward also across the lower lip. Superimposed on this structure there is further decussation, more superficially placed at each corner of the mouth. In this instance, the *triangularis menti* muscle, from below, tapers out rapidly at the corner of the mouth but extends into the upper lip. The *caninus* muscle, from above, projects itself downward and mingles to some extent with the *triangularis* muscle but in the main passes directly underneath this muscle to reach the lower lip. Both the *triangularis* and the *caninus* muscle are inserted into the skin near the midline. Immediately underneath the *triangularis* muscle, the *platysma* is inserted into the *orbicularis* fibers of the *sphincter oris*. Still superficial to the *platysma* at the corner of the mouth and slightly superiorly, the *zygomatic* and the *risorius* muscles also join the underlying muscle groups to form the thickening of the cheek in this general area. According to Henle, the *zygomatic* muscle is split into two layers at the corner of the mouth, thus forming a canal, in which the superior labial blood vessels are found. The superior and inferior *incisor labialis* muscles are also attached to this nodule, while the superior and inferior *quadratus labii* muscles are inserted more medially. Also deeply placed and still more medially are the *mentalis* muscle, of the lower lip, and the *nasalis* muscle, of the upper lip. The small muscles of Klein are short, sparse, fragmentary bundles which are situated in the lip proper, are placed at right angle to the *orbicularis* fibers and extend from these to the subcutaneous tissue. They are more frequent in the midline and become less in number in the lateral portions of the lips. This group of fibers is sometimes spoken of as the *compressor labii*.

The foregoing description of the *orbicularis* muscle was taken from the current anatomic textbooks, with liberal help from the older reports of Aeby<sup>7</sup> (1879) and Roy<sup>8</sup> (1890). With modern technical facilities for making serial sections and with the newer plastics for reconstructions, it may be possible to give a more complete idea of the way the different muscles contribute to the formation of the *orbicularis oris* muscle.

Embryologically, the *sphincter oris* muscle, being one of the muscles of expression whose evolution has been so well described by Ernst Huber in 1931, gradually becomes differentiated out of that mass of early muscle tissue which has its origin in the second or hyoid arch and is supplied by the facial nerve.

7. Aeby, C.: Die Muskulatur der menschlichen Mundspalte, Arch. f. mikr. Anat. 16:651, 1879.

8. Roy, J. P.: Le muscle orbiculaire des lèvres, Thesis, Bordeaux, no. 28, 1890.

The same terminology being used, the double harelip is generally described as being due to a bilateral lack of fusion between the maxillary and medial nasal processes in addition to an excessive protrusion of the premaxilla. It would seem that the lateral nasal process also did not fuse. Whether this time-honored explanation will survive is open to doubt because of recent and as yet unpublished work by Dr. George L. Streeter, Research Associate in Embryology, Carnegie Institution of Washington. His models and drawings, which I have had the privilege of seeing, give the basis for a different interpretation.

#### MATERIAL AND METHOD

Opportunity to study anatomically a case of double harelip was afforded by the Department of Embryology, Carnegie Institution of Washington.

The specimen, no. 5605 in the collection of the Department of Embryology, Carnegie Institution of Washington, was received on Dec. 20, 1927 from Dr. Harold Cummins, of the Department of Anatomy of the Tulane University of Louisiana College of Medicine. The marasmic Negro baby girl lived for five months. Besides the double harelip she had a cleft palate, together with partial and complete congenital amputations of the fingers of the right hand and toes of the right foot. The amputations were described by Dr. George L. Streeter<sup>9</sup> in a previous publication.

The entire body had a fixative crown to rump length of 343 mm. and was preserved in 10 per cent solution of formaldehyde.

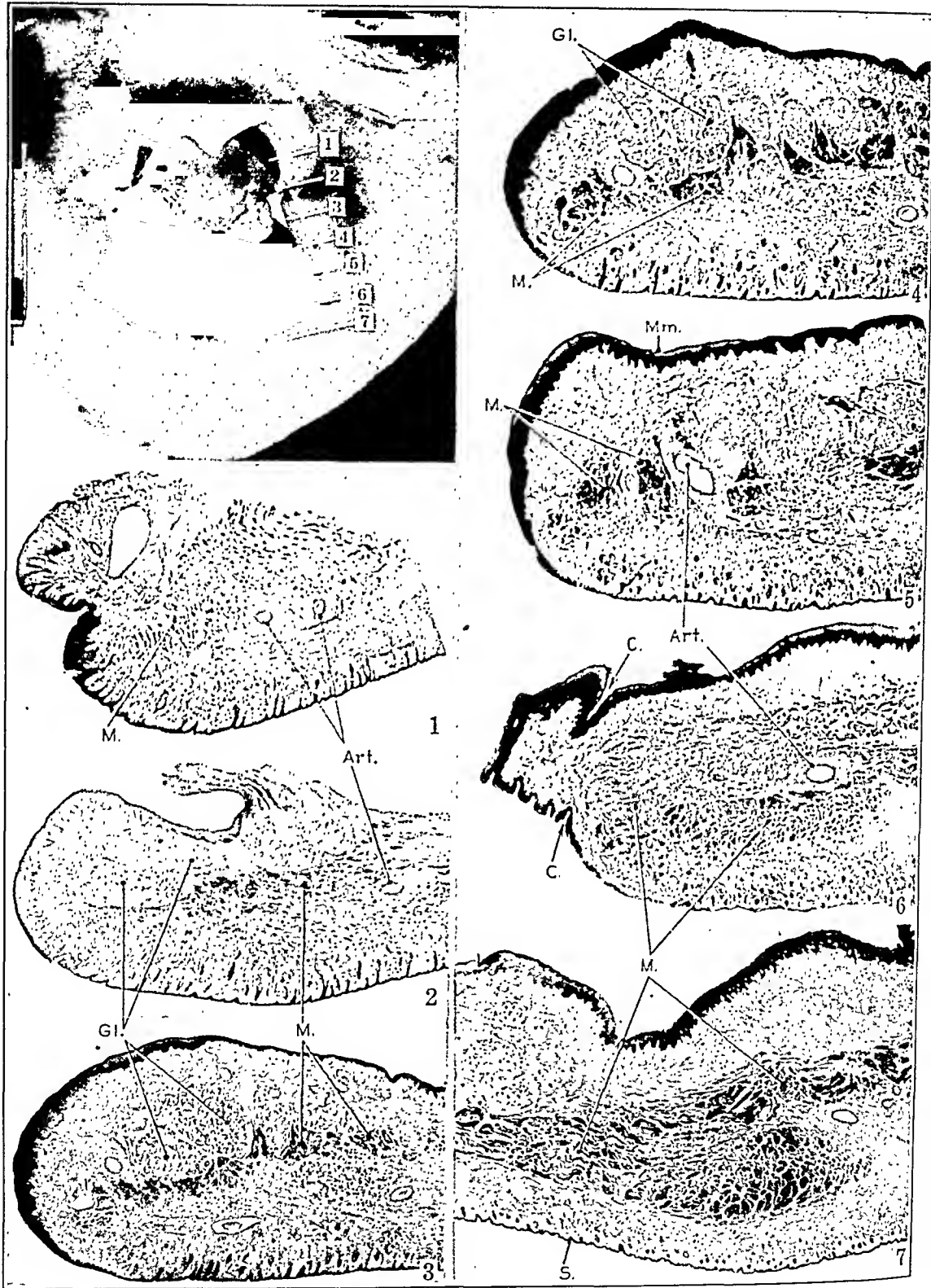
For the study of the orbicularis oris muscle, the entire left side of the upper lip together with a portion of the left side of the lower lip was removed in one piece, embedded in colloidin and serially sectioned at a thickness of 20 microns. Every tenth section was stained in hematoxylin and eosin and mounted in balsam. This pilot series forms the basis of the report.

In addition, the right half of the labial premaxilla was taken as one block, as were individual wedges of tissue from the right side of the upper lip in order to supply sections for purposes of control.

For convenience of description, section 6 in the accompanying illustration may be considered first. This section is at the corner of the mouth and contains the largest amount of striated muscle not only relatively but also actually as far as the upper lip is concerned. The superior labial artery marks the lateral border of the cross-sectioned vertical muscle fibers which form the bulk of the orbicularis oris muscle. However, the horizontal fibers, probably the buccinator muscle, extend

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9. Streeter, G. L.: Focal Deficiencies in Fetal Tissues and Their Relation to Intra-Uterine Amputation, *Contrib. Embryol.* **22**:1, 1930.



(See legend on opposite page)

still more laterally and occupy the entire posterior portion of the muscle mass; medially they almost reach the mucocutaneous border at the corner of the mouth, where they decussate, maintaining a horizontal position as far as the lower lip is concerned (section 7) but making a sharp vertical change of direction as they enter the upper lip (section 5).

Medial to the superior labial artery is a connective tissue septum, which extends halfway to the mucocutaneous juncture. It is only about 1 mm. wide and is immediately flanked by muscle bundles, which may be portions of the split zygomatic muscle, of which the anterior portion is the larger.

Section 6 being used as a base, several contiguous cylindric bundles of muscle, all about the same size, extend upward into the central vertical plane of the lip. These columns appear gradually at successively higher levels, the first one being placed laterally and the others following in a medial direction.

The first column, beginning anteriorly and medially to the superior labial artery, continues upward and slightly laterally, being displaced by the dividing artery and finally assuming a smaller size and a posterior position. At the same time the buccal glands, which are absent in the plane of section 6, begin to appear and not only to become rapidly larger, numerous and more anterior but also to engulf and split up the column of muscle, which thins out for a short distance but then becomes thicker as it spread laterally. The muscle wall restricts in general the buccal glands to a posterior position, which they keep. However, the wall, which takes on a scalloped appearance (section 3), not infrequently allows glands to penetrate and even reach a relatively subcutaneous position (sections 3 and 4).

The second column of muscle separates out as an entity soon after the first column has appeared and continues upward directly medially to the superior labial artery, and when this vessel divides the column maintains the same relative position except that now it is lateral to the medial branch of the superior labial artery. It then breaks up in small, narrow columns, which later become thicker and more numerous, with the lateral bundles blending with the medial segments of the first column. The buccal glands do not pierce this wall of muscle.

The third column of muscle differentiates out quickly once the second column has formed. The distance between the horizontal planes

#### EXPLANATION OF PLATE.

The muscle tissue in a 5 month old baby with a double harelip. Photograph of face, showing the position of the seven serial sections. *M.* indicates muscle; *Gl.*, buccal glands; *Art.*, artery; *S.*, skin; *C.*, corner of mouth, and *Mm.*, buccal membrane. The sections are magnified 8 times.

of origin of the first and third columns is about 0.8 mm. Like the second and third columns, many of the muscle fibers of the third column are derived from the buccinator muscle, of which some fibers continue horizontally anteriorly and medially to form a less distinct fourth column, which is near the mucocutaneous border of the lip.

The third column continues upward and then takes a more anterior position, being anterior and medial to the medial branch of the superior labial artery. Gradually this column becomes less compact and thinner, with its lateral segments running parallel to the contiguous medial portions of the second large column of muscle. At the same time the third column of muscle retreats a little from the medial plane but still maintains a relatively close position to the cutaneous position of the lip. Finally, the fiber bundles become only gradually more and more attenuated, until at the uppermost portion of the lip they quickly become thin, few and scattered.

The fourth column, as previously mentioned, is small, quickly turns upward, always is near the mucocutaneous junction and blends with the third column. It is about 2.4 mm. in length.

In section 2 the four columns of muscle have lost their individuality, but they still maintain a line which holds the buccal glands in a posterior position. The increased frequency of longitudinally cut fibers suggests the influence of the quadratus labii superioris muscle. The dearth of muscle near the mucocutaneous border indicates a lateral displacement of the muscle columns.

In section 1 the muscle columns have entirely disappeared, and the muscle tissue is in numerous, widely dispersed small muscle bundles situated relatively deep to the skin. Buccal glands are scant, and hyaline cartilage appears.

Below the corner of the mouth, it will be seen from section 7 that the mass of muscle is primarily the buccinator and caninus muscles situated posteriorly, with the triangularis muscle predominating anteriorly. Buccal glands are also present.

#### COMMENT

In presenting actual photographs of sections taken through the lip of a person who had a double harelip, a more accurate record is available than if a composite drawing had been made.

To what extent normal structures, like the buccinator muscle, contribute to the formation of the orbicularis muscle in an abnormal condition like a double harelip can only be conjectured. Accordingly, no claim is made for the accuracy in the explanation of the participation of specific muscles.

Study of the serial sections of the corner of the mouth of this 5 month old specimen casts some doubt on the structure of the adult

orbicularis oris muscle as pictured in the anatomic textbooks. These books show a heavy development of concentric sphincter muscles at the angle of the mouth. The specimen of this report showed almost the exact opposite, namely, relatively few sphincter muscle bundles but a heavy mass of horizontal fibers which extend close to the free border of the lip.

The buccal glands in volume may occupy as much as a quarter of the entire lip in the upper sections. In the lower sections, near the corner of the mouth, many of the glands are partly surrounded by muscle columns, which, through their contractions, might add appreciably to the emptying mechanism of the glands.

The loose distribution of the muscle bundles, together with the absence of well developed perimysial membranes, recalls the anatomic basis for the rapid spread of an acute infection of the upper lip.

#### SUMMARY

In order to study the orbicularis oris muscle, serial sections were made of the left side of the upper lip of a 5 month old human specimen having double harelip.

It was found that this muscle is well developed at the corner of the mouth but quickly becomes thin and fragmented as the ala of the nose is reached. It is moderately effective in forming a barrier to keep the buccal glands in a posterior position in the lip.

No support was found for the view that there is a large concentration of purely sphincter muscle fibers at the corner of the mouth.

The Department of Embryology, Carnegie Institution of Washington, and its director, Dr. George W. Corner Sr., as well as his predecessor, Dr. George L. Streeter, contributed the material on which this report is based.



## FATALITIES FOLLOWING WAR WOUNDS OF THE ABDOMEN

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SINCE the ending of World War II many papers have been published dealing with abdominal injuries in warfare. Emphasis has been placed on patients that survived operation. This paper is presented as an analysis of the extent of injury and the cause of death of those who did not survive intra-abdominal injuries.

This material was obtained from records of an active evacuation hospital and from two surgical teams working with active field hospitals. All autopsies in cases of death in the evacuation hospital were done by a pathologist attached to the unit. In the field hospitals, autopsies were done by an operating surgeon and were therefore limited because of the heavy burden thrust on the surgical teams.

In this series of patients there were 91 deaths following major abdominal wounds, and in 75 per cent of this group autopsies were performed. All patients had suffered major visceral and/or vascular damage. All thoracoabdominal injuries have been excluded. It will be noted that many of the patients in this series had other major associated wounds, such as compound fractures, injuries of the head and traumatic amputations.

Four hundred and forty-three patients with intra-abdominal wounds were operated on by us or under our direction. There was an operative mortality of 16.7 per cent. Two hundred and eighty-four patients with penetrating wounds of the abdomen were admitted to the evacuation hospital. Seventeen, or 5.6 per cent, died without operation. Of 877 patients with penetrating wounds of the abdomen admitted to the field hospital where many of these operations were performed, 57, or 6.49 per cent, died before operation could be undertaken. We feel that the latter figures are more important than the operative mortality. The low preoperative mortality indicates that little selectivity was exercised and that a high percentage of seriously wounded patients were given the small chance that operation could offer. Many of these patients were moribund on admission, usually as a result of overwhelming hemorrhage or severe peritonitis. Others were admitted with wounds incompatible with life despite operation. A few died while waiting for operation, as a result of a large preoperative reserve,

which on occasions was as high as 400 patients. It is probable that a few in the latter group might have been saved if operation could have been undertaken earlier. It will be noted later in the paper that many patients were sent to the operating room although it was doubtful that they would survive the operation. The deaths following the induction of anesthesia were listed as postoperative deaths.

Sixty-three of this series of nonsurvivors were American soldiers, 20 were prisoners of war and 8 were allied or enemy civilians. The percentage of bullet wounds (38 per cent) is higher in this series than that stated by Cutler<sup>1</sup> for war wounds in general (29 per cent) seen in the First United States Army. Imes<sup>2</sup> reported bullet wounds in 22 per cent of his series of penetrating wounds of the abdomen. Shell fragments (artillery, mortar, bomb and grenade) caused 58 per cent of the wounds, and 4 per cent remained unclassified in this series.

#### SHOCK

Sixty-five of the 91 patients who died were admitted in profound shock. Almost half (30 patients) responded poorly or not at all to the usual treatment with whole blood, plasma, arrest of visible hemorrhage and splinting of fractures. The cause of the shock could not be ascribed to any one factor except in occasional instances but, for the most part, was a combination of hemorrhage, evisceration of abdominal contents, severe intraperitoneal contamination and what Hardt and Seed,<sup>3</sup> and Jolly<sup>4</sup> referred to as the "retroperitoneal syndrome."

Hemorrhage was the outstanding feature of nearly one third (20 patients) of the patients admitted in severe shock. The diagnosis of shock due to hemorrhage in patients with multiple severe concomitant injuries was not difficult. The additional diagnosis of severe intra-abdominal hemorrhage in such patients frequently presented a difficult problem. Failure to respond to the liberal use of whole blood within two hours was usually considered sufficient evidence to suspect intra-abdominal hemorrhage. Patients thus suspected frequently were found at operation to have peritoneal cavities full of blood but with no active bleeding present. The manipulation of exploration or repair of intraperitoneal injuries usually dislodged clots which revealed the location of an injury to a major vessel.

1. Cutler, E. C.: *Military Surgery, United States Army, European Theater of Operation, 1944-1945*, Surg., Gynec. & Obst. **82**:261, 1946.

2. Imes, P. R.: *War Surgery of the Abdomen*, Surg., Gynec. & Obst. **81**:608, 1945.

3. Hardt, H. G., Jr., and Seed, L.: *Thoracoabdominal Gunshot Wounds*, Arch. Surg. **46**:59 (Jan.) 1943.

4. Jolly, D. W.: *Field Surgery in Total War*, New York, Paul B. Hoeber, Inc., 1941.

Eighteen (19.8 per cent) patients had abdominal viscera protruding from the peritoneal cavity. The accompanying contamination, drag on the mesentery and impairment of blood supply to the viscera involved were factors which made this complication respond poorly if at all to supportive therapy, even in the absence of accompanying severe hemorrhage. The high mortality (63.8 per cent) of this serious complication is pointed out by Bradford and colleagues.<sup>5</sup>

The most consistent contributing factor to shock was severe fecal contamination of the peritoneal cavity, occurring in about 70 per cent of the cases. Patients with severe peritoneal contamination alone frequently survived, with remarkably smooth convalescence. Accompanied with multiple severe injuries, severe hemorrhage or extensive retroperitoneal damage, it often provided sufficient additional insult to produce a fatality.

Jolly<sup>4</sup> has described a syndrome of retroperitoneal injury accompanied with severe shock in the absence of excessive bleeding or peritoneal contamination. He stated the belief that the shock is of neurogenic origin. Two of our patients may possibly fall into this group. Both, however, had severe fecal contamination of the retroperitoneal tissues.

#### REPORT OF CASES

CASE 1.—An American soldier sustained a gunshot wound (machine gun) of the right side of the lower part of the abdomen. On admission eleven hours later, his pulse was imperceptible and his blood pressure was below 80 systolic. Administration of 1,500 cc. of blood and 500 cc. of plasma produced no significant improvement during the next six hours, and with the patient under anesthesia by bilateral intercostal block celiotomy was undertaken.

There was no significant intraperitoneal fecal soiling, but the retroperitoneal portion of the cecum was severely lacerated and there was an extensive laceration of the retroperitoneal tissues. The kidney was undamaged, but there was a small compound fracture of the right wing of the ilium at the site of the wound of exit. A cecostomy was carried out and the retroperitoneal tissues débrided and drained. The patient withstood the procedure well but remained in shock and succumbed twelve hours following operation. Clinically, the case was not considered a case of renal failure.

CASE 2.—An American soldier sustained a gunshot wound (rifle) of the right side of the lower part of the abdomen. He was admitted within three and one-half hours, in severe shock. During the preoperative administration of 1,000 cc. of blood and 250 cc. of plasma his blood pressure continued to fall, and intra-abdominal hemorrhage was suspected. Two and one-half hours after admission, he succumbed during the operative procedure. Autopsy revealed only minimal hemorrhage and no injury except a lacerated cecum with severe retroperitoneal damage and considerable fecal contamination to the retroperitoneal tissues. There was no gross or microscopic evidence of renal damage.

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5. Bradford, B., Jr.; Battle, L. H., and Pasachoff, S. S.: Abdominal Surgery in an Evacuation Hospital, *Ann. Surg.* **123**:32, 1946.

It can be seen in table 1 that 16, or 17 per cent, of the patients had major vascular injuries within the abdomen. All were associated with visceral injuries except in 3 instances. Twenty-eight per cent had three or more intra-abdominal organs injured. Seventy-eight per cent had two or more organs injured. Twenty-two per cent had only

TABLE 1.—*Tabulation of Abdominal Organs Injured*

| Organs Injured  | No. of Cases |
|---|--------------|
| Colon, small intestine.....                                     | 20           |
| Small intestine .....   | 11           |
| Colon, small intestine, bladder.....                            | 8            |
| Colon .....   | 7            |
| Colon, great vessel.....  | 6            |
| Colon, kidney .....   | 5            |
| Small intestine, bladder.....                                   | 3            |
| Colon, small intestine, great vessel.....                       | 3            |
| Great vessel .....  | 3            |
| Kidney .....  | 3            |
| Colon, bladder .....  | 2            |
| Colon, liver .....  | 2            |
| Colon, small intestine, liver.....                              | 2            |
| Small intestine, great vessel.....                              | 2            |
| Stomach .....   | 2            |
| Liver, kidney .....   | 2            |
| Colon, small intestine, stomach.....                            | 1            |
| Colon, small intestine, liver, kidney.....                      | 1            |
| Colon, small intestine, liver, bladder.....                     | 1            |
| Small intestine, kidney .....                                   | 1            |
| Small intestine, great vessel, bladder.....                     | 1            |
| Stomach, liver .....  | 1            |
| Stomach, liver, kidney, pancreas.....                           | 1            |
| Liver .....   | 1            |
| Liver, kidney, great vessel.....                                | 1            |
| Blast (subserosal hemorrhage of the colon and small intestine). | 1            |

one organ injured. It is important to note that 72 per cent of this series had other major associated lesions, such as compound fractures, injuries of the head or extensive wounds of the soft tissues. For these patients, who survived transport to the nearest hospital, this

TABLE 2.—*Associated Major Injuries*

| Injuries  | No. of Cases |
|---|--------------|
| Compound fracture of long bones.....  | 36           |
| Extensive damage to the muscles (buttock, thigh).....                                   | 27           |
| Compound fracture of pelvis.....  | 20           |
| Multiple severe lacerations.....  | 16           |
| Compound fracture of vertebrae.....   | 11           |
| Penetrating wound of brain.....   | 5            |
| Major vessel lacerated or divided, with impairment of blood supply to an extremity..... | 5            |
| Traumatic amputation of an extremity.....   | 4            |
| Trench foot, severe.....  | 1            |

factor of multiplicity of severe injuries was responsible for far more deaths than the severe damage of one vital organ. An analysis of major injuries other than intra-abdominal is shown in table 2.

CASE 3.—An American soldier sustained wounds by high explosive shell fragments. He was admitted eleven hours later, at which time his blood pressure was unobtainable and pulse imperceptible. He was pale and had constant

nausea. Administration of 500 cc. of blood in 500 cc. of Alsever's solution<sup>6</sup> was begun immediately, but soon afterward the patient had a violent reaction to the transfusion. One thousand cubic centimeters of plasma was given. Following its administration, his blood pressure rose to 104 systolic and 78 diastolic and his pulse rate to 120. In the meantime clinical and roentgenologic examination revealed the following wounds:

1. Penetrating wound of the abdomen
2. Compound fracture of the left femur
3. Compound fracture of the left tibia and fibula
4. Compound fracture of the right radius and ulna
5. Compound fracture of the right scapula
6. Severe lacerations of the left thigh and lower part of the leg
7. Penetrating wounds of the right thigh, scrotum, penis and neck
8. Foreign bodies (by roentgenologic examination) in neck, right upper quadrant of abdomen, pelvis and at site of all compound fractures

Operation was carried out ten hours after admission, at which time the patient had twelve perforations of the small intestine closed. All wounds were débrided and appropriate plaster encasements applied. The patient had 500 cc. of blood and 500 cc. of plasma during operation. He remained anuric during his post-operative period and succumbed fifty-four hours after operation. Autopsy revealed the following additional significant findings: (1) pulmonary infarction in the lower lobe of the right lung, (2) hemoglobinuric nephrosis and (3) moderate peritonitis. We believe that this patient received too little blood. The cause of death was undoubtedly due to renal ischemia on the basis of (a) prolonged inadequately treated shock and (b) violent reactions to transfusions:

#### SURGICAL PROCEDURE

Thirteen (17.5 per cent) of the patients on whom some major surgical procedure was carried out died during operation. A few of these severely injured patients died during the induction of anesthesia, but the deaths were considered operative deaths. Later in the campaign, anesthesia by bilateral intercostal block was used rather than the inhalation type on the patients who presented bad risks. This substantially reduced the operative mortality in this type of patient, though it may have had little effect on the ultimate outcome in the case. On the 75 patients operated on the following procedures were done:

|  | No. of Patients |
|--|-----------------|
| Exteriorization of wounded large bowel.....                              | 40              |
| Resection of small intestines, with anastomosis.....                     | 27              |
| Repair of lacerations of small intestine.....                            | 27              |
| Débridement and immobilization of compound fractures of long bones ..... | 25              |
| Suprapubic cystotomy and repair of bladder.....                          | 11              |
| Ligation of great vessel.....  | 9               |
| Liver packed .....   | 5               |
| Repair of the colon (distal to colostomy).....                           | 4               |
| Nephrectomy .....  | 4               |
| Amputation .....   | 4               |
| Liver sutured .....  | 3               |
| Kidney sutured .....   | 3               |
| Repair of stomach.....   | 3               |
| Craniotomy .....   | 2               |
| Resection of colon.....  | 2               |
| Repair of ureter.....  | 1               |
| Repair of great vessel.....  | 1               |
| Incision and drainage of intraperitoneal abscess.....                    | 1               |

6. Alsever's solution contains 0.80 per cent sodium citrate, 2.05 per cent dextrose and 0.42 per cent saline solution in an isotonic solution of sodium chloride.

Loria<sup>7</sup> has emphasized the importance of the operating time. In his series of cases the mortality was considerably higher when the operating time exceeded one and one-half hours. The length of time a patient is subjected to anesthesia and the trauma of operation are of considerable importance. The difference in mortality in our experience was not due to length of the operation but to the severity and number of the injuries.

#### PREOPERATIVE DEATHS

Sixteen patients died without benefit of operation. Several factors were responsible for this. The condition of the patient and seriousness of the injury, the rapidity with which death followed the patient's admission to the shock ward and our inability to operate on every patient at the optimum time, due to a reserve of seriously injured patients, are the most important factors. For example, 50 per cent died within four hours after being admitted to the shock ward and one-half of this number within one hour. Obviously, most of these patients would have succumbed had operation been undertaken during this period.

The problem of how much shock therapy these moribund patients should receive, especially in relation to the number of hours following injury or admission, and the availability of operating room space and personnel become, at times, extremely complex. It is the natural inclination of every surgeon or triage officer in choosing between 2 seriously injured patients for operation to choose the one who has made a satisfactory response to shock therapy and to allow the pulseless, pressureless patient to receive more blood, with the hope that his response may be a delayed one. If this patient then succumbs after four or five or more hours in the shock ward, some criticism may be leveled at persons responsible for allowing him to remain unoperated on for so long. Most surgeons, in our experience, made a constant and conscientious effort to operate on all the patients presenting bad risks as soon as possible. The patients not responding to shock therapy for suspected hemorrhage were given the highest priority, regardless of risk.

A few patients suffered more than the usual delay in being returned to the hospital, because of the tactical situation and as a result often were more completely exsanguinated than their more fortunate companions. This seemed especially true in cases of prisoners of war who obviously had to be overrun and captured before being returned to a hospital for medical attention. An additional factor was the apparent policy of the enemy to leave behind the severely wounded persons on evacuation of a position. These factors account, to some

7. Loria, F. A.: Penetrating Gunshot Wounds of Abdomen, *South. M. J.* 36:87, 1943.

extent, for the high percentage of prisoners of war (43 per cent) in this group in which no operation was performed.

A more detailed analysis of this group of patients may be found in table 3.

#### CAUSE OF DEATH

Insofar as possible an attempt was made, either at clinical examination or at autopsy, to determine the cause of death. In classification of the cases, considerable overlapping of contributing factors was present. The patients who died as a direct result of hemorrhage presented no particular problem.

A great number of patients, however, without an excessive amount of hemorrhage were admitted in a state of shock and died shortly after operation, apparently as a result of shock. They may or may not have responded satisfactorily to the usual supportive measures. All of them had severe, widespread, intraperitoneal fecal contamination, which, in our opinion, was the chief factor in contributing to their death. Such patients have been listed in table 4 under "shock and acute peritonitis." This is not to imply that all such patients succumbed, for persons with experience in either World War I or World War II can undoubtedly recall many similar patients who made remarkably smooth recoveries.

Patients who failed to survive because of widespread peritonitis are classified in table 4 under "peritonitis." These, for the most part, were patients with severe peritonitis who survived for a few days and then succumbed. Their pathologic process was purely one of infection, and the entire clinical and pathologic picture unassociated with shock. Frequently these patients had continuous sources of contamination, such as an overlooked hollow visceral perforation or a suture line that had failed to hold.

Two cases were classified under "retroperitoneal syndrome," previously discussed.

Hemolytic reactions to transfusions were thought to be responsible for death in 6 cases, and in 4 cases microscopic sections of the kidney were diagnosed as hemoglobinuric nephrosis. The reports on the other 2 cases were never received from the laboratory, but from the clinical and gross pathologic findings they fell into the same group.

Seven patients were believed to have died from pulmonary complications. All were reported to have had pneumonia. In addition, 3 had evidence of lobular infarction, but no patient was found to have died from a massive pulmonary embolus.

Associated major injuries were responsible for 5 cases of death, in 3 of which the patients never reached operation. These included cases of a severely damaged brain, an infected compound fracture of

TABLE 3.—*An Analysis of Cases in Which Operation Was Not Performed*

| Nationality and/or Status of Patients | Interval Between Injury and Admission, Hr. | Interval Between Admission and Death, Hr. | Extent of Abdominal Injury   | Significant Associated Major Injuries  | Cause of Death, Based on Autopsy Findings                    | Comments  |
|---------------------------------------|--|---|--|--|--|---|
| German civilian                       | ?  | 20  | Severe laceration of pelvic colon  | Severe lacerations of buttocks; compound comminuted fracture of vertebrae  | Peritonitis  | Obvious severe peritonitis on admission                               |
| French civilian                       | ?  | 4   | ?  | Penetrating wounds of buttocks, arm and scrotum  | No autopsy   | On admission thought to have intra-abdominal hemorrhage               |
| American Prisoner of war              | 1  | 14  | Laceration of vena cava  | None   | Hemorrhage   |   |
| Prisoner of war                       | ?  | 48  | Laceration of superior mesenteric vessels  | None   | Hemorrhage   |   |
| Prisoner of war                       | ?  | 20  | Laceration of common iliac vein; penetrating wound of rectum                               | Compound comminuted fractures of ilium and hand  | Hemorrhage   |   |
| Prisoner of war                       | 12   | 1½  | Laceration of ilioocolic artery; perforating wound of cecum and ileum                      | Compound comminuted fractures of ilium and hand  | Hemorrhage   |   |
| Prisoner of war                       | ?  | 43  | Penetrating wound of cecum, sigmoid and ileum  | Compound comminuted fractures of sacrum, ilium, femur, radius and ulna   | Severe peritonitis   | Blood pressure never above 60 systolic                                |
| American                              | 4  | 25  | Evisceration of ileum and transverse colon; perforating wounds of colon, jejunum and ileum | None   | Severe peritonitis   | Blood pressure and pulse always unobtainable; comatose                |
| American                              | ?  | 1   | Perforating wound of cecum and ascending colon   | Severe penetrating wound of brain  | Severe damage to brain                                       |   |
| American                              | 2 days                                     | 6½ days                                   | One perforation of ileum   | Infected compound comminuted fracture of femur   | Severe infection; compound fracture of femur; no peritonitis | Incision and drainage of the thigh; hip spica; observation on abdomen |
| Prisoner of war                       | ?  | 3   | Transection of sigmoid, colon and ileum  | Compound comminuted fracture of ilium; penetrating wound of buttocks   | Severe peritonitis   | No tourniquet in place on admission                                   |
| American                              | 5  | 1/12                                      | Perforating wound of stomach   | Compound comminuted fracture of tibia and fibula; severed anterior and posterior tibial arteries and radial and ulnar arteries | Hemorrhage   |   |
| Prisoner of war                       | ?  | ¼   | Perforated ileum and colon; lacerated mesenteric vessels                                   | Compound comminuted fracture of ilium  | Hemorrhage   |   |
| Prisoner of war                       | ?  | 3   | Severe laceration of kidney  | Compound comminuted fracture of vertebra   | Hemorrhage   |   |
| American                              | 4 days                                     | 24  | Perforating wound of ileum, colon and bladder  | Compound comminuted fracture of femur, radius and ulna and pelvis  | Severe peritonitis   |   |



the femur and an exsanguination from lacerated vessels of the extremities. A severely damaged brain and gas gangrene of the buttocks accounted for the 2 deaths from associated injuries in the group in which operation was performed.

Eight cases were listed as "unclassified." Included in this category were 1 case of death from the anesthetic (pentothal sodium); 1 case in which the patient was reported to have died from aspiration of a large quantity of vomitus; 1 case of death from blast; 1 case in which sudden death occurred following removal, on the seventh postoperative day, of a large hepatic pack and in which autopsy revealed no explanation for the death; 1 case in which death followed dehiscence of a wound and abdominal evisceration on the eighth postoperative day, and 3 cases in which no cause of death could be determined.

TABLE 4.—Cause of Death

| Cause                                  | Total Cases | Operated On | Not Operated On |
|--|-------------|-------------|-----------------|
| Shock and hemorrhage.....              | 21          | 13          | 8               |
| Shock and acute peritonitis.....       | 19          | 19          | 0               |
| Peritonitis.....                       | 23          | 18          | 5               |
| Hemolytic reaction to transfusion..... | 6           | 6           | 0               |
| Retroperitoneal syndrome.....          | 2           | 2           | 0               |
| Pulmonary complications.....           | 7           | 7           | 0               |
| Associated major injuries.....         | 5           | 2           | 3               |
| Unclassified.....                      | 8           | 8           | 0               |
|  | 91          | 75          | 16              |

#### ERRORS OF SURGICAL JUDGMENT

It is inevitable that some errors will be committed in the management of nearly 450 patients with penetrating wounds of the abdomen. Many were patients for whom treatment was difficult and in whom a certain percentage of error may have been excusable. Others were committed under the burden of an extremely heavy load of patients or other trying conditions. Obvious errors in this series of patients who died fall into the following groups:

|   | No. of Patients |
|---|-----------------|
| Unrecognized penetrating wounds of the abdomen..... | 2               |
| Overlooked perforations of hollow viscera.....      | 6               |
| Improper use of pentothal sodium.....               | 1               |
| Failure to apply a tourniquet.....                  | 1               |

Many patients conceivably could have been called mishandled, because they were taken to the operating room before or after the optimum time for operation. The amount of shock therapy a patient should receive is a relative matter and depends largely on the tentative diagnosis. Patients with suspected hemorrhage not responding to shock therapy were operated on much sooner than those without the probability of severe hemorrhage.

Two patients had unrecognized penetrating wounds of the abdomen. Neither had wounds penetrating the abdominal wall, the wound of entry having been in the thigh in both patients.

CASE 4.—An American soldier was admitted forty-eight hours after injury. His only wound was a severe compound comminuted fracture of the middle and lower third of the left femur. The muscles of the thigh were badly damaged. At the time of admission, frank pus was present in the wound and the soft tissues were edematous and friable. Roentgenologic examination accidentally revealed a small shell fragment in his pelvis, probably within the peritoneal cavity. His condition was poor, but there was no clinical evidence of peritonitis or intra-abdominal bleeding. Incision and drainage of the thigh, with application of a plaster encasement, was carried out. Celiotomy was considered but decided against because of the extremely poor condition of the patient. His course was continually downhill, and he died three days later.

Autopsy showed a single perforation of the ileum, which had effectively sealed itself off and was surrounded only by a small area of localized peritonitis. Death was attributed to sepsis as a result of extensive infection of the thigh.

CASE 5.—An American soldier was received as a transfer from a field hospital on his third postoperative day. He previously had had débridements of compound fractures of the femur and radius. Roentgenologic examination also revealed a fractured pelvis. From the record, celiotomy had not been considered. At the time of admission, his condition was extremely poor and he had evidence of generalized peritonitis. He died twenty-four hours after admission.

Autopsy revealed severe generalized peritonitis with multiple perforations of the ileum, sigmoid colon and urinary bladder.

One of the dangers of a "too hurried" operation is an overlooked perforation of a hollow viscus. Severe intraperitoneal hemorrhage and extensive concomitant injuries necessitate a lengthy operative procedure. A tendency to "speed through" a seemingly untouched corner of the abdomen is usually responsible for such errors. Hamilton and Duncan<sup>8</sup> in discussing overlooked perforations, reported an incidence of 30 per cent in 30 autopsies. Other authors report somewhat higher figures:

|   | Percentage | No. of Autopsies |
|---|------------|------------------|
| Oberhelman and LeCount <sup>9</sup> ..... | 55.5       | 169              |
| McGowan <sup>10</sup> .....               | 55.5       | 27               |
| Taylor <sup>11</sup> .....                | 43         | 14               |
| Billings and Walking <sup>12</sup> .....  | 19         | 49               |
| Rippy <sup>13</sup> .....                 | 50         | 12               |
| Willson <sup>14</sup> .....               | 50         | 20               |

8. Hamilton, J. E., and Duncan E.: Penetrating Gunshot and Stab Wounds of the Abdomen, *Surgery* **13**:107, 1943.

9. Oberhelman, H. A., and LeCount, E. R.: Peacetime Bullet Wounds of the Abdomen, *Arch. Surg.* **32**:373, 1936.

10. McGowan, F. J.: Penetrating Wounds of the Abdomen, *Ann. Surg.* **102**:395, 1935.

11. Taylor, F. W.: Gunshot Wounds of the Abdomen, *J. Indiana M. A.* **31**:342, 1938.

12. Billings, A. E., and Walking, A.: Penetrating Wounds of the Abdomen, *Ann. Surg.* **94**:1018, 1931.

13. Rippy, E.: The Management of Perforating Gunshot Wounds of the Abdomen, *South. Surgeon* **10**:441, 1941.

14. Willson, F. C.: Gunshot Wounds of the Abdomen, *South. M. J.* **27**:805, 1934.

When cases in which operation was not performed and those in which death occurred during operation are excluded, in 6 of 38 cases which came to autopsy in our series perforations of a hollow viscus were found to have been overlooked, an incidence of 15.8 per cent.

The 1 death attributed to anesthesia was considered to be an error. In a soldier having a severe wound of the abdomen with evisceration but with only moderate shock, 0.25 Gm. of pentothal sodium was used for induction of anesthesia. The patient quickly succumbed, and all efforts to resuscitate him failed.

One patient became exsanguinated from hemorrhage of lacerated vessels of the extremities. He was admitted without a tourniquet in place, and from his record no tourniquet had been applied. The instruction so frequently given to medical officers and their corpsmen in the forward areas concerning the unwarranted sacrifice of limb as a result of application of tourniquets may have allowed some to become overcautious in their use, and this may possibly be considered an example.

#### SUMMARY

1. An analysis of 91 cases of death from intra-abdominal injury seen in evacuation and field hospitals of the First United States Army is presented. Seventy-five per cent of the cases came to autopsy.

2. Approximately 5 per cent of patients dying after receiving abdominal wounds died without operation having been undertaken.

3. Nineteen and eight-tenths per cent of the patients who died had evisceration of abdominal contents on admission to the hospital. Nearly three fourths of the patients had concomitant major injuries.

4. Seventeen and one-half per cent of this group died during operation.

5. The causes of death and errors in surgical judgment are discussed.

# PRODUCTION OF EXPERIMENTAL PORTAL HYPERTENSION IN THE DOG

Anatomy of the Hepatic Veins in the Dog

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**V**ENOUS congestion of the liver by constriction of the posterior vena cava anterior to the kidneys has been produced by others.<sup>1</sup> Death generally follows five to ten hours after the complete ligation of the cava just above the renal veins.<sup>2</sup> If the animal survives, such a procedure results in congestion not only of the hepatic and portal systems but also of the systemic regions drained by the cava caudad to the obstruction, particularly the kidney. The present work was undertaken with the object of producing hepatic congestion and accompanying portal hypertension in the dog, without the associated congestion of the systemic system.

When the experiments were undertaken, a number of difficulties in the attainment of this objective became apparent. These arose from the fact that in the dog no satisfactory description of the anatomic relationships of the hepatic veins and of their relation to the posterior vena cava was available in the published literature. A special study of these relationships was, therefore, carried out.

Forty-six livers were used in the anatomic studies. Five hardened livers were dissected in which the vena cava had been injected with a colored gelatin mass. In addition, one corrosion preparation was made, in which the posterior vena cava and the hepatic veins, down to the small tributaries, had been filled with a solution of Vinylite in

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This work was carried out in the departments of Experimental Surgery and Anatomy, New York University College of Medicine, and was aided by a grant from the Dazian Foundation for Medical Research.

1. (a) Montemartini, G.: *Contributo sperimentale all chirurgia della vena cava inferiore*, *Polielinico (sez. chir.)* **41**:593 (Nov.) 1934. (b) Rohde, G.: *Die Stauung der unteren Hohlvene von dem rechten Herzen und ihre Bedeutung im Krankheitsbilde der Pericarditis adhaesiva*, *Deutsche Ztschr. f. Chir.* **203**-**204**:18 (May) 1927. (c) Zimmerman, H. M., and Hillsman, J. A.: *Chronic Passive Congestion of the Liver*, *Arch. Path.* **9**:1154 (June) 1930.

2. Whittenberger, J. L., and Huggins, C.: *Ligation of the Inferior Vena Cava*, *Arch. Surg.* **41**:1334 (Dec.) 1940. Montemartini.<sup>1a</sup>

acetone. Forty freshly removed livers were dissected without any special preparation. While the number of livers is admittedly not large, the surprising fact emerged that little variation was encountered in the cases studied. The accompanying diagram (fig. 1), with the exception of the slight variation noted in the following material in the drainage of the papillary lobe, might have been made directly from any one of the livers.

In the following description the terms of position employed are those in common use in comparative anatomy, "dorsal" and "ventral" being

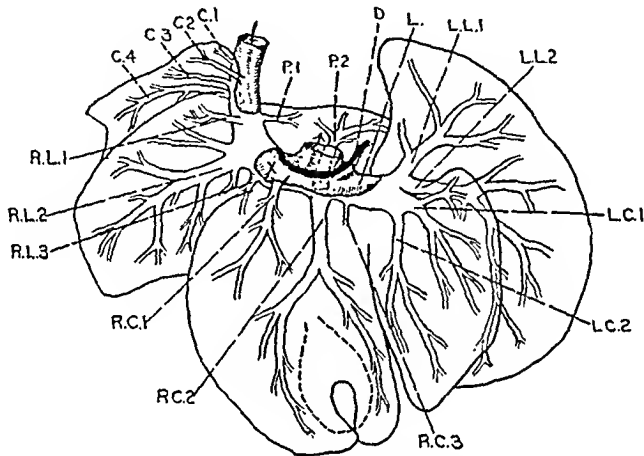


Fig. 1.—Diagrammatic anterior view of the dog's liver, represented as a transparent object, to show the pattern of the hepatic veins. The liver has been spread somewhat, to obtain a view of its entire parietal outline. Unshaded veins are within the hepatic substance. The shaded portions represent venous surfaces not in contact with liver. The solid black band crosses the vena cava where that vessel pierces the diaphragm. The arrows indicate the direction of blood flow through the vena cava. The broken line indicates the outline of the gallbladder. *C.* indicates the caudate lobe, *P.* the papillary lobe, *R. L.* the right lateral lobe, *R. C.* the right central lobe, *L. C.* the left central lobe and *L. L.* the left lateral lobe. Further explanation is in the text.

synonymous with the "posterior" and "anterior" of gross human anatomic terminology and "anterior" and "posterior" with the "superior" and "inferior" respectively of the latter.

✓ The posterior vena cava is lodged in a deep groove on the dorsal aspect of the right lobe. In all the livers examined, this groove was converted into a tunnel for about the last half inch (1.2 cm.) just posterior to the diaphragm, by the presence of a thin bridge of hepatic tissue passing dorsal to the vena cava, between the right lateral and papillary lobes (fig. 1). From the superoventral surface of the right central lobe the peritoneum is reflected not directly onto the diaphragm but first onto the vena cava, so that this portion of the vein may be seen through the peritoneum in the living animal if the liver is depressed and the diaphragm raised (marked X in figure 1).

The course of the posterior vena cava, where the vein is in contact with the liver and hence capable of receiving hepatic veins, may be conveniently divided into three parts. Of these, the first is intimately related to the caudate lobe; the second is the portion previously noted as being entirely surrounded by hepatic substance and hence is related to the right lateral and papillary lobes, and the third part immediately precedes the passage of the vein through the diaphragm. It is intimately related to the right central and papillary lobes and includes the portion of the vessel previously noted as being visible through the peritoneum, between the liver and the diaphragm.

In the first part of its course the vena cava receives four veins, of somewhat variable size, which enter its lateral aspect and constitute the entire drainage of the caudate lobe (*C1 to C4*, fig. 1). In the second part of its course the vena cava receives laterally three veins from the right lateral lobe and medially one from the papillary lobe. Of the three veins draining the right lateral lobe, the second is by far the largest, conveying most of the blood from that lobe. The vein from the papillary lobe is of variable size and in no case constitutes the entire drainage of that lobe. In the last part of its course, before piercing the diaphragm, the vena cava receives two veins from the right central lobe; of these, the second is the larger (*R.C. 2*, fig. 1) and drains the entire area of the gallbladder. It also receives a vein from the papillary lobe (*P.2*) and a large vein, which is here called the left hepatic vein (*L*, fig. 1).

The drainage of the papillary lobe constitutes the only variable of importance seen in the study. In 1 case the entire drainage of this lobe was into the third part of the vena cava. In all others the drainage was partly into the second part (*P.1*) and partly into the third (*P.2*). In 1 case these two hepatic veins were of approximately equal size, while in the remainder the vein joining the third part of the vena cava (*P.2*) was the larger.

The left hepatic vein joins the vena cava almost at right angles to the course of the latter. At its termination it is not entirely enclosed by liver but, like the cava itself, is covered anteriorly only by peritoneum and may be clearly seen in the living condition through the peritoneum, where that membrane is reflected from the diaphragm onto the antero-ventral surface of the liver. The left hepatic vein constitutes the entire drainage of the left lateral and left central lobes. It is formed within the liver, at the base of the cleft separating these two lobes, by the junction of a large vein from each. Each of these veins is, in turn, a short trunk formed by the junction of two veins from its own lobe (*L.L.1* and *L.L.2* and *L.C.1* and *L.C.2*, fig. 1). Just before it enters the vena cava the left hepatic vein receives a small tributary from the medial margin of the right central lobe (*R.C.3*). At its point of junction with

the vena cava, the left hepatic vein further receives a vein of considerable size, which emerges from the substance of the diaphragm (*D. fig. 1*).

On the basis of these anatomic findings, no practical experimental approach on the hepatic veins directly suggested itself. In some early experiments, Winternitz<sup>3</sup> ligated the hepatic veins in the dog and found no changes in the liver. In 1925 Simonds and Brandes<sup>4</sup> reported a method of producing experimental portal hypertension in the dog by occluding the hepatic veins without interfering with the blood flow through the posterior vena cava. Briefly, their method consisted in passing one end of a rubber tube (Rehfuss stomach tube) along the right side of the falciform ligament, between the liver and the diaphragm, through the membranous portion of the triangular ligament, thence through the epiploic foramen, up through the membranous portion of the left triangular ligament and along the left side of the falciform ligament, between the liver and the diaphragm. In this way, when the two ends of the tube were approximated, all the hepatic lobes were included within the loop. By exerting traction anteriorly and caudad on the ends of the rubber tube and at the same time producing counterpressure on the hepatic substance between the limbs of the tube, they claimed that it was possible to constrict the hepatic veins as they enter the posterior vena cava without lifting the liver out of its bed and so to avoid constriction of the vena cava. They offered as proof of this contention the observations that there is no distention of the femoral veins and that peptones, when injected into the femoral veins of experimental animals, produced systemic effects as rapidly as in control animals.

More recently, Armstrong and Richards<sup>5</sup> carried out similar experiments, but with some modification. They passed an occlusive ligature through the foramen of Winslow, forward over the left dome of the liver, around the anterior edge of the falciform ligament and backward over the right dome of the liver. To reduce the occluded tissue to a minimum the triangular ligaments were divided. The tie was made at the foramen of Winslow, and the ligature was left in place. Only 3 of the 9 dogs operated on survived. The remaining 6 died from hemorrhage caused by an inadvertent tear of the liver, from simultaneous occlusion of the posterior vena cava or from complete rapid occlusion of only the hepatic veins.

Several attempts were made to produce venous congestion of the liver by the method of Simonds and Brandes in the experiments herein described. None of the 46 dogs examined had a falciform ligament.

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3. Winternitz, M. C.: The Effect of Occlusion of the Various Hepatic Veins upon the Liver, *Bull. Johns Hopkins Hosp.* **22**:396 (Nov.) 1911.

4. Simonds, J. P., and Brandes, W. C.: The Effect of Obstruction of the Hepatic Veins on the Systemic Circulation, *Am. J. Physiol.* **72**:320 (April) 1925.

5. Armstrong, C. D., and Richards, V.: Results of Long Term Experimental Constriction of the Hepatic Veins in Dogs, *Arch. Surg.* **48**:472 (June) 1944.

In about half the dogs there was a fragile, fibrous cord extending from the umbilicus to the portal fissure; this probably was an obliterated umbilical vein. In addition, when the operation was carried out a kinking of the posterior vena cava always occurred, presumably due to the fact that for part of its course the cava is completely surrounded by hepatic tissue. In these experiments there was little distention of the femoral veins, although the vena cava was completely occluded at the base of the liver. This lack of distention appears to be related to the existence in the dog of collateral venous pathways which are capable of returning the blood to the heart with little or no delay (see figure 2*B*).



Fig. 2.—Infra-red photographs of 1 normal (*A*) and 1 experimental animal (*B*), showing extensive development of collateral circulation after the production of portal hypertension.

In view of the existence of so efficient a collateral circulation and because of the complicated anatomic arrangement of the hepatic veins in relation to the posterior vena cava, it was decided to try to produce venous portal congestion without associated systemic congestion by a three stage procedure. This method involves ligation of the vena cava immediately caudad to the liver in two stages. By the use of such a procedure, the collateral pathways for returning blood to the heart are allowed to come into full play, thus preventing systemic congestion after the vena cava is completely occluded or severed completely. In the third stage the posterior vena cava anterior to the liver is partially occluded, in this way insuring the development of portal congestion.



## METHOD

Dogs ranging in weight between 9.5 and 21 Kg. were anesthetized with pentobarbital sodium administered intravenously. The abdomen was opened by a midline incision and the posterior vena cava exposed. The point of entrance of the adreno-renal veins was located and the cava followed upward under the liver. A ligature was passed around the wall of the cava above the point of entrance of the renal veins and tied (fig. 3, stage I), constricting the lumen of the vessel approximately 70 to 80 per cent. The abdomen was closed in layers. This completed the first stage of the procedure.

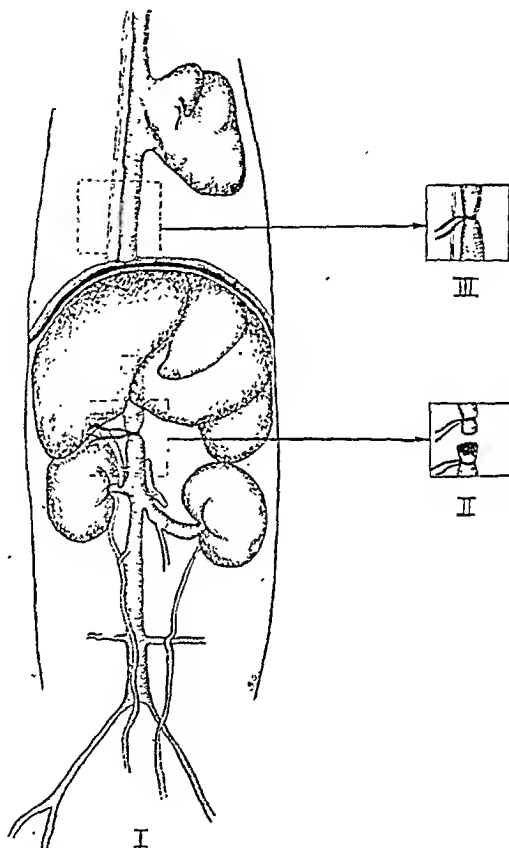


Fig. 3.—Schematic representation of the three stages in the operational procedure for producing venous portal hypertension. Stage II is carried out four or more weeks after stage I, and stage III is done three or more weeks after stage II.

After four weeks or longer the animal was again operated on. The cava was doubly clamped and cut at the site of the partial occlusion. The cut ends of the vessel were ligated with suture ligature (fig. 3, stage II) and allowed to retract as they were dropped back. This step constituted the second part of the procedure.

The third and final stage was carried out three weeks or more after the second stage. With the dogs under intratracheally administered cyclopropane anesthesia, a portion of the ninth rib was resected and the right pleural cavity was opened. The posterior vena cava was identified, and the right phrenic nerve, which runs along with the vein at this point, was dissected free. A ligature was placed around

the cava and tied to occlude the vessel approximately 70 to 80 per cent (fig. 3, stage III). The thoracic wound was closed in layers as the lung was reinflated.

Early in this work an attempt was made to occlude the posterior vena cava between the liver and the diaphragm and thus to avoid entering the pleural cavity, but in several instances in which this step was undertaken it was found that the ligature instead of encircling the cava and the hepatic veins, which are closely associated at this site, actually pierced the vessels. This did not become apparent until autopsies were done on the animals and the exact position of the ligature determined. Because of this uncertainty and other difficulties attendant on ligation of the vessels in this manner, this procedure was abandoned in favor of the one already described.

After the feasibility of the foregoing approach was demonstrated, reference to a similar method, by Soskin and colleagues,<sup>6</sup> was found. These investigators studied the role of the liver in the maintenance of blood sugar level and the movement of sugar into and out of the liver. They prepared the dogs by a preliminary two stage ligation of the posterior vena cava just below the liver. They then measured the blood flow in the thoracic portion of the posterior vena cava and used that as an index of the total blood flow through the liver. In the dogs examined during the present investigations a large diaphragmatic vein emptying into the left hepatic vein at its junction with the third portion of the cava was always found. Thus, not all the caval blood came from the liver.

#### RESULTS

Forty-six dogs were used in the experiments to be described. The first 3 dogs were used in attempts to produce venous congestion of the liver by ligation directly of the hepatic veins draining the various lobes of the liver. In no instance could a uniform state of congestion be obtained by this method. One dog was subjected to the procedure of Simonds and Brandes<sup>4</sup> for the temporary occlusion of the hepatic veins. The animal was killed with the constricting tube in place in order to obtain precise information concerning the position of the tube and to determine the patency of the posterior vena cava. In 1 dog the vena cava was completely severed and ligated without preliminary partial occlusion. This dog died after twelve hours. In 1 case a lumbar approach to the posterior vena cava was tried and found to be less satisfactory than the intra-abdominal route.

Thirty-nine dogs were subjected to the first stage of the procedure as outlined under the section on methods. Twelve of these died before the second stage. The first animal operated on died of hemorrhage

6. Soskin, S.; Essex, H. E.; Herrick, J. E., and Mann, F. C.: The Mechanism of Regulation of the Blood Sugar by the Liver, *Am. J. Physiol.* **124**:558 (Nov.) 1938.

from the liver. Of the remaining 11 dogs, 7 had no immediate post-operative complications. In 3 of this group infected wounds developed, which eventually led to their death eleven, nineteen and thirty days after operation, and 2 died of *Clostridium welchii* infection two and thirty-seven days after operation. Of the remainder, 2 died of distemper, in 1 mange developed and the animal died ninety-six days after operation, 1 was destroyed by fire in the kennels and 1 died of eating poisoned food. None of these deaths could be attributed directly to the circulatory readjustments brought about by occlusion of the posterior vena cava 70 to 80 per cent.

The second stage of the procedure was carried out on 23 dogs. In 2 instances the posterior vena cava had been completely occluded by the first operation. It is, therefore, possible to occlude completely the vena cava without preliminary partial constriction and to have an occasional animal survive. Two dogs died as a direct result of the operation, 1 of hemorrhage from the liver and the other from failure to recover from the anesthetic. Five other dogs died postoperatively; 3 died of *Cl. welchii* infection five, twelve and fifty-seven days after the stage II operation, and 1 dog died on the ninth postoperative day, after a large hematemesis, but the exact site of bleeding could not be found at necropsy. In the remaining dog, the attachment of the diaphragm at the ensiform cartilage was cut in making the abdominal incision and a pneumothorax was produced, resulting in death from pneumonia twenty-one days later.

Stages II and III (intra-abdominal method) were combined into one operation in 4 cases. In no instance did the ligature of the cava cephalad to the liver produce the desired effect of constriction by complete encirclement.

The stage III intra-abdominal procedure was carried out as a separate operation on 5 dogs. One died of *Cl. welchii* infection forty-seven days after the third stage. Necropsy again revealed that the ligature did not produce constriction. An interesting and most unusual finding in this animal was a small canalized endothelial tube containing blood, which had bridged a gap of 2 cm. between the cut ends of the severed vena cava. Two dogs died one and ten days after stage III, from hemorrhage from the vena cava and the liver. In both animals the ligature had passed through the lumen of the posterior vena cava and not around the vessel. In 1 dog there was considerable bleeding from a torn hepatic vein; this was controlled by ligature, and the animal survived. Because of the results obtained, the intra-abdominal route for stage III was abandoned and it was decided to constrict the cava cephalad to the liver in the thorax.

The thoracic approach to the posterior vena cava was attempted on 8 animals. Three dogs died on the operating table, from the anesthetic.

The remaining 5 dogs were successfully operated on, and the posterior vena cava constricted approximately 70 to 80 per cent in the thorax, immediately cephalad to the diaphragm. One of the dogs died of empyema six days after the last operation. The 4 remaining dogs survived for much longer periods and were used in extensive physiologic and chemical studies. The dogs all showed pronounced development of the collateral veins on their ventral aspect. Figure 2 shows 1 normal and 1 experimental animal as viewed by infra-red photography. One of these dogs died three months after the stage III operation. The animal did well up to about a week before it died; at that time it became progressively weaker and more sluggish until it finally expired. Necroscopy showed the posterior vena cava in the thorax almost completely occluded. The kidneys appeared mottled, the spleen small and the stomach dilated. In another one of these dogs a large ventral hernia developed. The animal was anesthetized with open drop ether in order that this hernia might be repaired and it died as a result of anesthesia before any operation was carried out. This was almost seven months after the stage III operation. At necroscopy it was found that the encircling ligature constricted the thoracic portion of the posterior vena cava about 60 per cent. The azygous vein was almost as wide as the vena cava. The liver was normal in size; it was dark in color (bluish black) and adhered to all the surrounding viscera; in section it was gritty. The pancreas was normal and the spleen smaller than normal, with no adhesions. The stomach was small. The small intestine adhered to the dorsal part of the abdominal wall. The veins in this region were extremely distended. The kidneys appeared congested, although the renal veins were normal in size. The two remaining dogs were killed after all the physiologic experiments were completed.

#### COMMENT

A procedure has been devised for production of venous congestion in the dog mechanically, a three stage operation being used. This method, in contrast to earlier methods, has the advantage of avoiding the congestion of systemic regions caudad to the occlusion. It does so by taking into account the complex nature of the relationship between the hepatic veins and the posterior vena cava and by making use of the collateral circulation from the caudal regions of the body to the heart, in this way preventing caudal congestion.

That portal hypertension occurs in animals subjected to the operational procedure described has been noted in extensive physiologic studies carried out on many of the dogs and especially on the 4 animals that survived all the operations. These studies, together with chemical analysis, will be reported on in detail in a forthcoming publication. However, some of the more general effects of the operational procedures

will be discussed at this time. The portal pressure is increased after the first operation. By partial occlusion of the postcaval vein caudal to the liver increased portal resistance is built up and the blood is forced into channels which are inconspicuous under normal conditions. These anastomoses connect the portal and systemic veins and thereby promote a path for the return of blood from the splanchnic area to the right side of the heart.

After the new collateral circulation has developed stage II can be performed, with minimum damage to the kidneys.

With the performance of stage III the portal blood pressure is increased still more. With an original pressure of about 8 cm. of water, there is no filtration from the capillaries into the abdominal viscera. With increased pressure of 15 cm. or more of water, there is increased filtration. The slow rise in pressure is evidenced by the latent period of the development of ascites after the posterior vena cava has been partially occluded below the heart. Ascites in these animals was not observable until seven to twenty days postoperatively. Increasing quantities of ascitic fluid were formed as measured by changes in weight and by the large quantities of fluid that could be withdrawn.

#### SUMMARY

1. The anatomic relationships between the hepatic veins and the posterior vena cava in the dog are described.

2. A method for the mechanical production of venous congestion of the liver and accompanying portal hypertension has been devised.

Valuable help and cooperation in this work were received from Dr. Donal Sheehan, Professor of Anatomy, and Dr. Frank W. Co Tui, Associate Professor of Experimental Surgery.

## CARCINOMA OF PANCREAS STILL LOCAL AT AUTOPSY FOUR YEARS AFTER PALLIATIVE OPERATION

HARRY C. SALTZSTEIN, M.D.

AND

JOHN RAO, M.D.

DETROIT

Mattie A., aged 38, was admitted to Mercy Hall Cancer Hospital on March 9, 1945. She had been operated on at Woman's Hospital by Dr. W. E. Johnston in July 1941. Dr. Johnston, Dr. Don M. Beaver and Dr. Frances Ford supplied the notes from the latter hospital admission.

Prior to her admission to Woman's Hospital the patient had complained of pain and tenderness underneath the right costal margin for one year and of jaundice for two weeks. She had weighed 90 pounds (40.8 Kg.) and had a hemoglobin content of 69 per cent and a red blood cell count of 3,250,000.

At abdominal exploration on July 25, 1941, the head of the pancreas had been found to be the size of a large plum, round and hard. The gallbladder had been distended and the common duct dilated. There had been no evidence of disease of the gallbladder.

Cholecystogastrostomy had been done and a specimen for biopsy taken from the pancreas. Microscopic examination had revealed a "new growth consisting of anaplastic epithelial cells having a ductal differentiation. The diagnosis was adenocarcinoma of the head of the pancreas (ductal in type) of malignancy grade 2" (fig. 1).

The jaundice had disappeared twenty-one days after the operation and the patient had gone home. She had evidently been fairly well for three and a half years since the operation, was doing her own housework and felt strong. However, during the past eight months, i. e., since August 1944, she had failed. There had been edema of the legs since July 1944. She had not eaten well and had lost 49 pounds (18 Kg.). She had evidently been on a deficient diet in that she never ate any fruit or drank any milk.

General examination on admission to Mercy Hall Cancer Hospital on March 9, 1945 revealed a thin, emaciated woman. Abdominal examination was noncontributory except for scars of a previous laparotomy.

A blood cell count showed moderate anemia, a red blood cell count of 3,200,000, with 62 per cent (10.5 Gm. per hundred cubic centimeters) hemoglobin, and a white blood cell count of 6,350. Roentgenograms revealed a defect in the pyloric portion of the stomach, close to the duodenum, which was thought to be due to pressure from an extragastric mass. The stomach itself showed no intrinsic lesion.

Her course in the hospital was further downgrade. She appeared mentally deficient, said many foods were not good for her and seemed lethargic, weak and not interested in her surroundings; she died three weeks after entrance, on April 29, 1945.

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From Mercy Hall Cancer Hospital and Tumor Clinic.

Autopsy revealed a large adenocarcinoma involving the head and midportion of the pancreas (fig. 2). It was a nodular grossly spherical tumor mass 8 by 10 cm. in diameter but was entirely local and could be shelled away from the smaller distal portion, or tail, of the pancreas. When removed, it left the bed of the pancreas clean and free; there were no fixed extensions which would have prevented resection, and there were no local or distant metastases.



Fig. 1.—Biopsy specimen of carcinoma of the pancreas obtained at laparotomy on July 25, 1941. Cholecystenterostomy was done. The patient lived in relative comfort for four years.

Microscopic examination revealed adenocarcinoma somewhat more malignant than that shown in the biopsy specimen taken at laparotomy in 1941 but still easily recognizable as the same cell type (fig. 3).

#### SUMMARY

A case of carcinoma of the pancreas is presented which was proved by laparotomy and biopsy in 1941. In 1945, autopsy showed the tumor still local and apparently (as far as appearances at autopsy went) still resectable.

## COMMENT

Carcinoma of the pancreas is notoriously a disease of short duration from the onset of the symptoms to death. The total lapse of time between these two events is given as six months (Cecil<sup>1</sup>), six to eighteen months (Cyclopedia of Medicine, Surgery and Specialties<sup>2</sup>), six to eight months

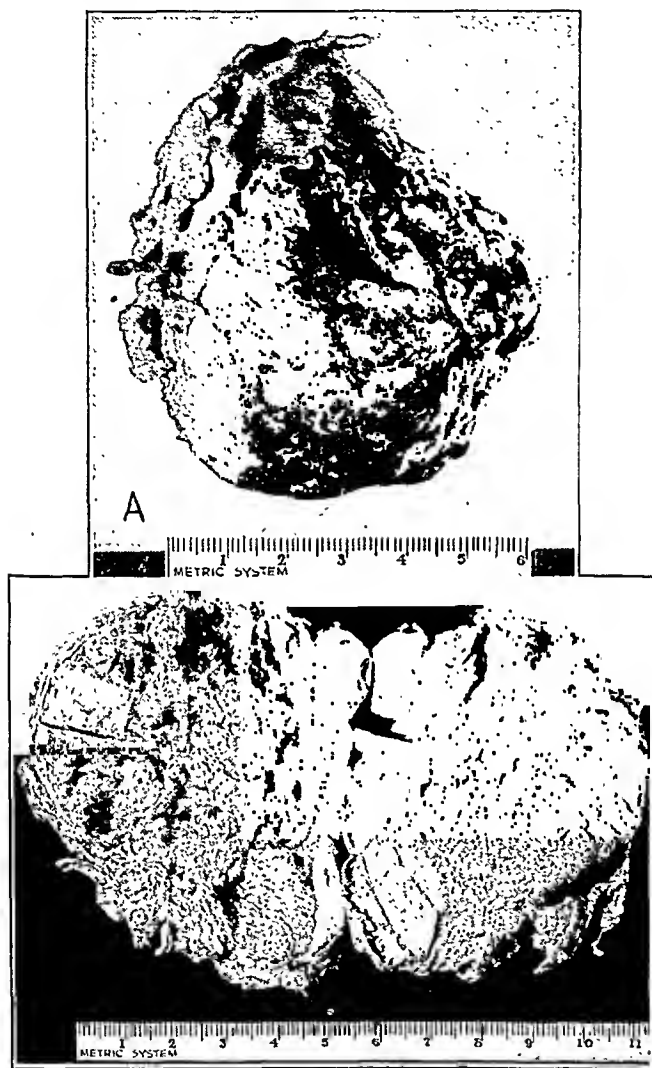


Fig. 2.—*A*, outer surface of a tumor of the pancreas removed at autopsy April 29, 1945. It involved the head and midportion of the pancreas and could be shelled out, leaving a clean bed without local extension. There were no metastases. *B*, cut section of the tumor.

1. Cecil, R. L.: Text-Book of Medicine, Philadelphia, W. B. Saunders Company, 1943, p. 979.

2. Piersol, G. M., and Bortz, E. L.: Cyclopedia of Medicine, Surgery and Specialties, Philadelphia, F. A. Davis Company, 1945, vol. 11, p. 120.



(Brunschwig<sup>3</sup>) and five to eight months, with the longest two years (Rives and colleagues<sup>4</sup>).

Ransom<sup>5</sup> reviewed 109 cases of cancer of the pancreas at the University Hospital of the University of Michigan Medical School in 1938. The average duration of symptoms before admission was five and one-half months, and the average length of life after palliative operation in

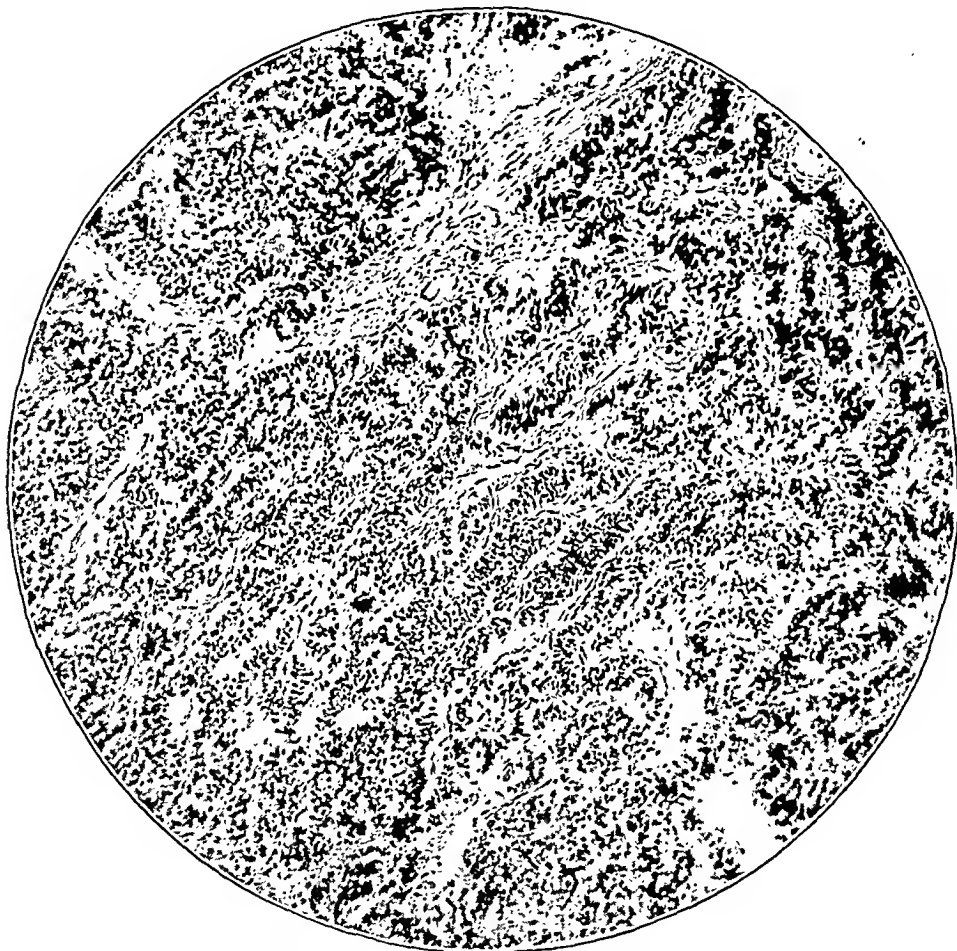


Fig. 3.—Microscopic section (autopsy specimen) of the tumor. Note similarity with figure 1.

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3. Brunschwig, A.: Radical Resections of Advanced Intra-Abdominal Cancer, *Ann. Surg.* **122**:923 (Dec.) 1945.

4. Rives, J. D.; Romano, S. A., and Sandifer, F. M., Jr.: Carcinoma of Pancreas, *Surg., Gynec. & Obst.* **65**:164 (Aug.) 1937.

5. Ransom, H. K.: Carcinoma of Pancreas and Extrahepatic Bile Ducts, *Am. J. Surg.* **40**:264 (April) 1938.

cases in that institution by a previous report (Coller and Winfield, 1934<sup>6</sup>) was 7.2 months.

Ransom stated: "In view of the notoriously rapid progress and relatively short life history of the disease, the histories of illness lasting over one year are perhaps open to question. In such instances it is quite possible that symptoms antecedent, such as gallbladder disease and peptic ulcer, may have merged with the earliest symptoms of cancer." He further stated that "long periods of relief of symptoms [following palliative operations] are occasionally reported. In such cases one is driven to the conclusion that the mass felt at the time of the operation was in fact inflammatory rather than neoplastic and that the internal drainage of the biliary tract resulted in a permanent cure."

Lahey<sup>7</sup> stated, "Many of these patients live comfortably for several months [following palliative short-circuiting operations] and occasionally two or three years before dying from the slow-growing carcinoma within the head of the pancreas." But, he added, "The length of time over which some of the patients upon whom we have done cholecystenterostomy for jaundice have lived can be explained . . . only by the fact that in some of the cases the obstruction was benign in character." Other authors have similarly expressed the feeling that in cases of long time arrests the obstructions were probably benign conditions rather than cancer.

We have not been able to find a proved case of carcinoma of the pancreas in which the patient lived four years after operation, such as happened in this patient. There are, however, occasional reports of cases of carcinoma of the pancreas which was still local at time of autopsy and in which, as far as gross autopsy appearances went, a radical resection might have been done.

Gordon-Taylor<sup>8</sup> stated, "In one case of my own, for which three palliative operations (!) of diverse nature had already been performed at another institution during the previous fifteen months and in which the diameter of the tumor was nearly 3½ in., the affected portion of the head of the pancreas was found at necropsy still to retain motility and showed no involvement of the portal vein or its parent tributaries, and there were no metastases."

In Ransom's series, in 30 autopsies five tumors originating in the biliary ducts were still localized, while two pancreatic cancers, one in

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6. Coller, F. A., and Winfield, J. M., Jr.: Evolution of Palliative Operation for Cancer of the Pancreas, *Am. J. Surg.* **25**:64 (July) 1934.

7. Lahey, F.: Carcinoma of the Pancreas, *S. Clin. North America* **17**:753 (June) 1937.

8. Gordon-Taylor, G.: The Radical Surgery of Cancer of the Lower End of the Common Bile Duct and Adjacent Pancreas, *Brit. M. J.* **2**:119 (Aug. 1) 1942.

the head and one in the body, were still local. Hick and Mortimer,<sup>9</sup> in 50 cases that came to necropsy, found 3 cases in which no metastases were found. These were cases of scirrhus carcinoma of the head of the pancreas. Rives and colleagues reported that 8 out of 96 patients were found at necropsy to have localized and resectable lesions.

The lesson clearly is that, with modern surgical improvements in technic and availability of large amounts of blood, there is a wider scope for operative removal. Involvement of the stomach, duodenum, middle colic vessels and even a portion of the portal vein are not absolute contraindications to wide removal. Such resections represent an attempt at cure or long time arrest, not palliation for a few months.

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9. Hick, F. K., and Mortimer, H. M.: Carcinoma of the Pancreas, *J. Lab. & Clin. Med.* **19**:1058 (July) 1934.

## PARA-ARTICULAR OSSIFICATION OF THE SOFT PARTS OF THE ANKLE

Complication of Sprain With or Without Fracture of the Shaft of the Ipsilateral Fibula

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**I**N 6 CASES of sprained ankle my colleagues and I noted the association of recurrent protracted episodes of pain and swelling of the part with ossification of local para-articular tissue.<sup>1</sup> In addition, there were 2 cases of sprain of the ankle with similar complications coexistent with fracture of the shaft of the ipsilateral fibula.

The clinical and roentgenographic findings in these 8 cases are presented to show the development of para-articular ossification about the region of the ankle and to stress its frequency.

### HISTORY AND SYMPTOMS

Three soldiers (group A), from 18 to 35 years of age, who came under our observation immediately after the advent of sprain of the ankle, experienced unusual prolonged convalescence. While a group of 42 other patients with sprain of the ankle made almost complete recoveries in from four to six weeks on routine treatment,<sup>2</sup> these 3 patients

1. Benassi, E.: Ossificazione post-traumatica paratibiale, *Arch. di ortop.* 45:409-415, 1929. Bistolfi, S.: Contributo allo studio della ossificazioni traumatiche para-articolari: le ossificazioni para-malleolari, *Arch. di radiol.* 8:566-604, 1932; Ulteriori osservazioni sulle ossificazioni post-traumatiche para-malleolari, con speciale riguardo alla diagnosi differenziale colle fratture parcellari, *ibid.* 9:1061-1081, 1933. Köhler, A.: *Röntgenology: The Borderlands of the Normal and Early Pathological in the Skiagram*, ed. 2, Baltimore, William Wood & Company, 1935. Pellegrini, A.: Ossificazioni post-traumatiche pararticolari (O.P.P.), *Arch. ital. di chir.* 53:501-563, 1938. Hempel, C.: Schalenförmiger Abbruch an der hinteren unteren Tibiafläche oder Verkalkung des Ligamentum malleoli lateralis posterius? *Deutsche Ztschr. f. Chir.* 258:100-102, 1943. Brailsford, J. F.: *The Radiology of Bones and Joints*, ed. 3, Baltimore, Williams & Wilkins Company, 1944. Piatt, A. D.: Post-Traumatic Para-Articular Calcifications and Ossifications of the Ankle, *Am. J. Roentgenol.* 54:348-356, 1945.

2. Treatment of simple sprain consisted in rest in bed and the application of cold compresses to the ankle for three to seven days. This was followed by a course of hydrotherapy, active exercises and weight bearing for periods from thirty to forty-five days. A rocker-bottom shoe was prescribed for at least the first thirty days of weight bearing. In instances in which complete tear of the fibuloastragalar ligaments was demonstrated by roentgenographic studies of the inverted astragalus, immobilization in plaster of paris boots was carried out.

complained of recurrent pain and swelling of the part from four to seven months after the onset of the sprain—the duration of the follow-up period. The injuries sustained by these 3 appeared to be similar in degree of severity to those suffered by the other 42 soldiers.

There were 3 other soldiers (group B), not included in the series of 42 patients, who also sought treatment for complaints of recurrent swelling and pain of a single ankle. They had suffered from sprain of the ankle from two to three years prior to their first visit to the orthopedic clinic.

Two soldiers (group C) who suffered from fracture of the shaft of the fibula with accompanying sprain of the ipsilateral ankle also complained of the pain and swelling of the joint before and after the removal of the plaster of paris boots. These symptoms reappeared several months after the occurrence of the sprain, in spite of hydrotherapy, graded exercises and limited activities.

#### PHYSICAL EXAMINATION

The examination of the 3 patients (group A) made soon after the onset of sprain of the ankle revealed the usual findings of ecchymosis, obliteration of landmarks by swelling, diffuse tenderness over the region of the ligaments and slight restriction in the range of active and passive movement of the foot. Reexamination of these 3 patients at intervals of one week for thirty-five days demonstrated the persistence of effusion, obliteration of landmarks, tenderness over the region of the posterior ligaments of the ankle and totals of 5 to 10 degrees of restriction in both active and passive dorsiflexion and plantar flexion of the foot. Examinations of these 3 patients (group A) made from four to seven months after the initial injuries disclosed moderate enlargement of the ankle and tenderness either on its medial or on its posterior surface. A total of 5 to 10 degrees of restriction in active and passive dorsiflexion and plantar flexion of the foot was again observed. Reexamination, made approximately four or more months after the sprain, revealed that avoidance of weight bearing for one or two days resulted in partial disappearance of the pain and swelling of the ankle. Recurrence of these symptoms was prompt after a short period of marching or hiking.

Examination of the 3 other patients (group B), who had suffered from recurrent swelling of an ankle for the past two to three years, disclosed partial obliteration of the normal landmarks, localized tenderness over the region of the posterior ligament of the affected part and totals of about 5 to 10 degrees of restriction in active and passive dorsiflexion and plantar flexion of the foot. On complete rest of the affected extremity for one or two days, the ankle presented almost normal appearance.

Examination soon after injury of the 2 patients with fracture of the shaft of the fibula (group C) revealed ecchymosis, swelling and tender-

ness of the leg as well as enlargement of the ipsilateral ankle. Movements at the ankle were painful and were restricted for totals of 10 to 25 degrees in active and passive dorsiflexion and plantar flexion of the foot. Reexamination made soon after the removal of the plaster of paris boots, from fifty to sixty days after the injury, disclosed moderate enlargement of the ankle. Localized tenderness was present over the posterior, lateral and medial aspects of the ankle. Follow-up studies made four or more months after the injuries disclosed that after complete rest of the extremity for one or two days there was a partial resolution of the swelling of the ankle. These 2 patients suffered considerably more from the swelling in the ankle than from the fracture of the shaft of the fibula.

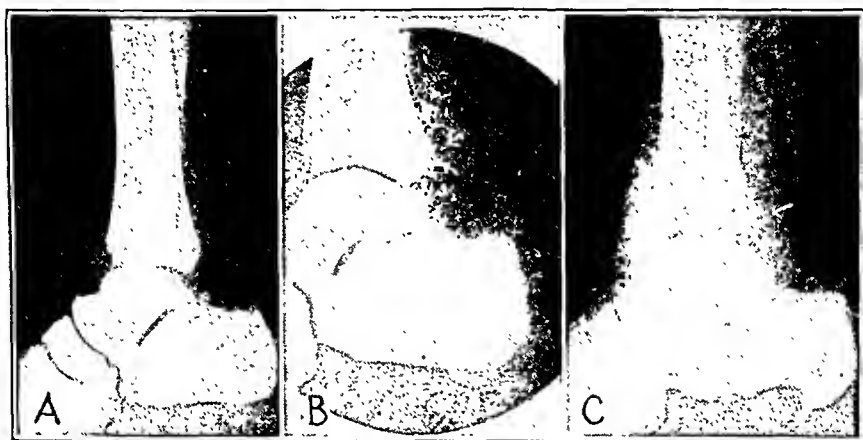


Fig. 1.—*A*, a roentgenogram taken soon after the occurrence of the sprain reveals swelling of the soft tissues of the region of the ankle (group A). *B*, a roentgenogram of the same ankle taken forty days later reveals an opaque plaque in the region of the posterior ligament (arrows). *C*, a roentgenogram of another ankle shows an opaque plaque in the region of the posterior ligament. This shadow made its appearance fifty days after the sprain (group A).

#### ROENTGENOGRAPHIC EXAMINATION

Roentgenographic studies made of the ankles of 3 patients (group A) soon after the occurrence of sprain showed no significant changes except local swelling of the soft tissues (fig. 1 *A*). Roentgenograms taken subsequently of these 3 patients, from forty to sixty days after sprain, demonstrated in each instance the presence of a small, thin vertical plaque of increased density in the region of the inferior transverse or posterior ligaments, just posterior to the distal extremity of the tibia. A clear or radiolucent zone existed between this area of increased density and the cortex of the tibia (fig. 1 *B* and *C*). In 2 of these 3 patients, areas of increased density were also present at this time in the

interosseous ligament, just proximal to the distal fibulotibial articulation. Roentgenograms of these parts taken from three to six months after the advent of the sprain revealed slight increase in the size and density of the radio-opaque shadows located in the interosseous and posterior ligaments. None of these opaque foci became attached to the fibula or tibia. These 3 soldiers presented no evidence of fracture, separation or subluxation of the bones comprising the ankle joint.

In addition, we had an opportunity to study roentgenographically 3 patients (group B) who had complained of swelling of the ankle for the past two to three years. Roentgenographic examination made of these 3 patients from two to three years after the initial sprain also demonstrated the existence of linear or elliptic-shaped plaques of increased density in the soft parts in the region of the distal end of the

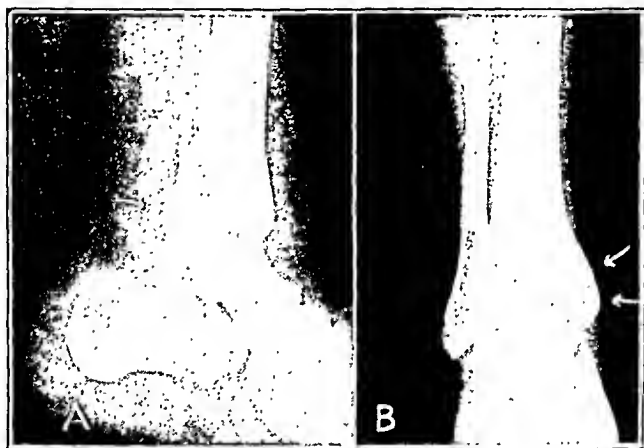


Fig. 2.—*A*, a roentgenogram of ankle reveals an opaque plaque in region of the posterior ligament. The patient (group B) has had recurrent local pain and swelling following a sprain of the ankle two years before. *B*, a roentgenogram of another ankle shows two opaque plaques in the region of the medial ligament. The patient (group B) has also experienced recurrent pain and swelling of the part for the past three years.

tibia. Two of these 3 soldiers presented densities which were situated in the vicinity of the inferior transverse or posterior ligaments (fig. 2 *A*). Roentgenograms of the ankle of the third patient revealed the presence of linear plaques of increased density in the para-articular region of the inner aspect of the medial malleolus of the tibia (fig. 2 *B*).

Another group, of 2 patients (group C), with fracture of the distal third and the upper third of the fibula respectively, also presented evidence of accompanying sprain of the ipsilateral ankle. Each of these 2 patients was immobilized in a plaster of paris boot for a period from fifty to sixty days. Within thirty days after the fracture of the lower third of the fibula, an opaque plaque was seen to form in the soft parts in

the locale of the inferior transverse or posterior ligaments of the ankle joint. In the other soldier, in whom the fracture had occurred at the upper third of the fibula, opacities were observed in the neighborhood of the inferior transverse or posterior ligament of the ankle within forty days after the initial injury. The formation of extra-articular bone in these 2 subjects was encountered during the period of immobilization of the leg and foot in the plaster of paris boot.<sup>3</sup>

#### TREATMENT

No attempt was made to remove the opaque plaques by surgical intervention. The soldiers in question were reassigned to duties which did not entail excessive walking or marching. They wore elastic bandage supports about the ankle and received repeated courses of hydrotherapy. This plan of treatment plus change in the status of duty resulted in definite partial resolution of the swelling and alleviation of the pain. In no instance, however, did the treatment which we pursued cause a disappearance of the radio-opaque plaques in the para-articular region of the ankle. The maximum period of follow-up of these 8 soldiers was twelve months.

#### COMMENT

The formation of dense plaques in the ligamentous structures about the ankle appears to be similar in character to that which takes place in the region of the tibial collateral ligament of the knee after trauma. Although para-articular ossification of the extremities may develop secondary to lesions of the spinal cord or of the peripheral nerves, no neurologic disturbances were present in these 8 patients.<sup>4</sup> We postulate that the complication described in this study is the result of ossification and not calcification of the connective tissue. This is not due to new periosteal bone but is probably secondary to healing of partly torn or stretched fibers of connective tissue about and in the ligaments of the ankle as well as in the interosseous ligament binding the fibula to the tibia. In 1 of the 8 patients, in whom a fracture had occurred at the upper third of the fibula in conjunction with a sprain of the ipsilateral ankle, the roentgenographic study of the ankle showed two distinct coexisting lesions (fig. 3). Firstly, a linear opaque plaque was noted

3. In another case of fracture of the fibular shaft and of the posterior margin of the distal end of the tibia with an incompletely fractured inner malleolus, we noted on roentgenograms made soon after the injury two linear spicules of bone detached from the cortex of the inner malleolus. This must be differentiated from para-articular ossification, which occurs approximately thirty or more days after the injury.

4. Suto, C. J., and Pomerantz, L.: Effect of Experimentally Formed Tumors on Musculoskeletal System of Rat, *Arch. Surg.* 38:1132-1149 (June) 1939.



in the region of the posterior ligament of the ankle, and secondly, formation of new periosteal bone was observed on the medial malleolus. This finding demonstrated that new periosteal bone caused by irritation of the periosteum can be differentiated roentgenographically from formation of para-articular bone.

The possibility that active movement of the affected ankle soon after the injury provoked formation of extra-articular bone can be ruled out. In 2 cases of fracture of the fibula with sprain of the ipsilateral ankle, we observed the formation of bone in the region of the posterior and medial ligaments during the period in which the affected leg and foot were immobilized in a plaster of paris boot.

As for the basis of the recurrent swelling of the ankle, we suspect that ossification in the region of the para-articular tissues caused secon-



Fig. 3.—A roentgenogram of an ankle (group C) reveals in the anteroposterior view formation of new periosteal bone on the inner malleolus. The lateral view shows a dense plaque in the region of the posterior ligament. Note the clear space between it and the cortex of the tibia.

dary inflammatory or irritative changes on the synovial surfaces of the contiguous capsules.

#### SUMMARY AND CONCLUSION

In 3 soldiers with protracted local pain and swelling of the ankle as the result of simple sprain of the part, we observed on roentgenographic study the formation of thin radio-opaque plaques in the region of the inferior transverse and posterior ligaments of the ankle. In 2 of these 3 patients, additional foci of ossification were noted in the vicinity of the interosseous ligament. These changes occurred under observation from forty to sixty days after simple sprain of the soft parts of the ankle.


In 3 other patients, in whom recurrent pain and swelling of the ankle had been present for two or three years after simple sprains, we noted on roentgenographic examination similar plaques of increased density in the region of the posterior or medial ligaments of the ankle.

Furthermore, in 2 other patients, with sprain of the ankle coexistent with fracture of the shaft of the ipsilateral fibula, similar developments of opacities in the region of the posterior ligament of the ankle were also observed.

Ossification of the connective tissue about and in these ligaments probably irritates the contiguous synovial lining of the ankle joint, with resultant effusion.

While ordinary sprain of the ankle usually affects the fibuloastragalar ligaments, it may also cause tears of parts of the interosseous ligament as well as of the inferior transverse, medial or posterior ligaments without resultant separation at the distal fibulotibial articulation. When such sprain is complicated by para-articular ossification, recurrent effusion and pain of the ankle may be intermittently present. Limitation of activity of the limb with the aid of a support about the ankle caused a partial resolution of the swelling and pain.

The clinical and roentgenographic picture of these 8 patients with para-articular ossification of the soft parts of the region of the ankle appears to be similar for the most part to that of ossification of the tibial collateral ligament of the knee.



## INJURIES OF THE THORACIC DUCT

Report of a Case of Chylothorax in Which the Patient Recovered  
After Ligation of the Thoracic Duct

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**C**HYLOTHORAX due to damage of the thoracic duct either in the neck or in the chest is of rare occurrence and carries a high mortality. The continuous loss of chyle, without replacement, results fatally. Shackelford and Fisher<sup>1</sup> in 1938 summarized the findings in 41 completely recorded cases collected up to that time. Seven additional cases were not included in their statistical study, because of insufficient data. The mortality was 47.5 per cent. Bauersfeld<sup>2</sup> in 1937 could find only 6 cases reported from this country. Dorsey and Morris<sup>3</sup> in 1943 added 12 more cases, bringing the total to 60, and in 1945 Florer and Ochsner<sup>4</sup> reported another; including the case reported in this paper, the total is in the neighborhood of 62.

While chylothorax is of rare occurrence, severance of the thoracic duct in the neck without chylothorax is not uncommon. On one occasion, I deliberately ligated the duct in doing a radical dissection of the neck for carcinoma of aberrant thyroid tissue, without ill effect, and I have had reports from other doctors on 3 cases in which injury occurred at the time of operation and was recognized. In 1 instance the duct was ligated following its injury while a deep-seated gland was being removed for biopsy. In another, it was sutured following a partial severance while the anterior scalene muscle was being cut. In the third case, an anastomosis to the proximal stump of the internal jugular vein was done following its severance in a radical dissection of the neck. In none of these cases was there any complication from the ligation of the duct.

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1. Shackelford, R. T., and Fisher, A. M.: Traumatic Chylothorax, *South. M. J.* **31**:766 (July) 1938.

2. Bauersfeld, E. H.: Traumatic Chylothorax from Ruptured Thoracic Duct Treated by the Intravenous Injection of the Aspirated Chyle, *J. A. M. A.* **109**:16 (July 3) 1937.

3. Dorsey, J. F., and Morris, G. E.: Traumatic Rupture of the Thoracic Duct with Chylothorax, *J. A. M. A.* **119**:337 (May 23) 1942.

4. Florer, R., and Ochsner, A.: Traumatic Chylothorax, *Surgery* **17**:622 (April) 1945.

## ANATOMY

The thoracic duct originates from the cisterna chyli at about the second lumbar vertebra, passes through the aortic hilus of the diaphragm, lying between the aorta and the azygos vein, and ascends in the same relative position, slightly to the right of the midline, crossing to the left at the junction of the last cervical and the first thoracic vertebra.<sup>5</sup> It ascends into the neck behind the carotid sheath, rising as high as  $2\frac{1}{4}$  inches (6 cm.) above the upper border of the sternum, and then curves downward to enter the subclavian vein near its junction with the internal jugular vein. Its location in the neck is not constant, and the frequent variations should keep the surgeon operating in the left side of the lower part of the neck constantly on his guard. The primitive ducts were phylogenetically paired right and left vessels that ascended the posterior mediastinum and emptied into both the right and the left subclavian vein. Numerous cross communications existed and subsequently atrophied, the somewhat devious thoracic duct remaining as the main channel. The embryonal remains probably play a part in the collateral circulation that develops after ligation of the duct.

It is often erroneously thought that ligature of the thoracic duct at the point of venous entrance accomplishes complete obstruction and will result fatally. Harrison<sup>6</sup> in 1916 cautioned against ligature and described a method of anastomosing the duct to a nearby vein. However, De Forest,<sup>7</sup> as early as 1907, advised its ligature, stating his belief that adequate collateral circulation developed. Lee<sup>8</sup> in 1922 reviewed the subject and demonstrated in animals an extensive collateral circulation. The rerouted chyle may enter the circulation through a right thoracic duct or through connections with the azygos or intercostal veins. Lee also observed lymphatic connections in the abdomen with the lumbar veins. Connections have also been reported in other abdominal veins, such as the renal and the mesenteric. It is actually extremely difficult to exclude entirely the entrance of chyle into the venous system. In 1937, Blalock and his associates<sup>9</sup> tried a variety of operations on some 74 animals and were able to produce

5. Grant, J. C. B.: *Method of Anatomy*, ed. 3, Baltimore, Williams & Wilkins Company, 1944.

6. Harrison, E.: On the Treatment of Wounds of the Thoracic Duct, *Brit. J. Surg.* 4:304, 1916.

7. De Forest, H. P.: The Surgery of the Thoracic Duct, *Ann. Surg.* 46:705, 1907.

8. Lee, F. C.: The Establishment of Collateral Circulation Following Ligation of the Thoracic Duct, *Bull. Johns Hopkins Hosp.* 33:21 (Jan.) 1922.

9. Blalock, A.; Robinson, C. S.; Cunningham, R. S., and Gray, M. E.: Experimental Studies on Lymphatic Blockage, *Arch. Surg.* 34:1049 (June) 1937.

complete blockage in only 3. From this discussion, it is evident that ligation of the thoracic duct is not a dangerous procedure. It is the continuous external loss of chyle that results fatally.

The importance of the thoracic duct has been recognized for well over a century. Among the functions of the lymph system is the transport of 60 to 70 per cent of the fat from the lacteals of the intestinal villi into the venous system. As chyle is a filtrate, it might be expected that its other constituents would resemble those found in blood serum. This is true, but in amounts usually smaller than in serum. The protein content varies between 1 and 6 Gm. per hundred cubic centimeters. Sugar, nonprotein nitrogen, urea and amino acids are about the same as serum. The cholesterol and calcium contents are perhaps slightly lower. Lymph also clots, but more slowly than serum, as the thromboplastin derived from blood platelets is poorly represented and there is a relative excess of antithrombin.

As it has been shown that lymph flow may range from 60 to 190 cc. per hour in the thoracic duct, depending on circumstances,<sup>10</sup> a tremendous loss of fluid and important body constituents may take place in a twenty-four hour period. Pressures in the thoracic duct vary and are influenced by such things as intraperitoneal pressure, intrathoracic pressure, inflammation and food but are higher than venous pressures, which promote the ready entrance of lymph into the veins at the base of the neck. On complete blockage of the duct high pressures develop, but they fall after the development of collateral circulation. Another function of the lymph system has been indicated by Co Tui and his associates.<sup>11</sup> In 1944, they demonstrated that it is an important pathway not only for the return of proteins from the capillary filtrates to the blood but also for the mobilization of proteins from depots in the body and therefore is an important aid in maintaining the volume of blood and proteins following hemorrhage.

Chylothorax may result from a variety of injuries which either directly or indirectly result in tears or severance of the thoracic duct.<sup>12</sup> In the order of frequency, the following were the causes in the 41 cases summarized by Shackelford and Fisher: crushing injuries, wounds by bullet or stab, fall from a height, blow on the chest, throw against the front seat of an automobile or sudden hyperextension. Injury following a full meal seems to be of some importance. Accumu-

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10. Drinker, C. K., and Yoffey, J. M.: *Lymphatics, Lymph and Lymphoid Tissue*, Cambridge, Mass., Harvard University Press, 1941.

11. Co Tui; Barcham, I., and Shafiroff, B. G. P.: Ligation of the Thoracic Duct and the Posthemorrhage Plasma Protein Level, *Surg., Gynec. & Obst.* **79**:37 (July) 1944.

12. Smith, D. D., and Woliver, E.: Traumatic Chylothorax, *Arch. Surg.* **43**:627 (Oct.) 1941.

lations of fluid on the right side are most frequent and commonly result from indirect injury, the site of break usually being just above the diaphragm. The slightly right-sided position of the duct in the greater part of the chest is given as the reason for this. Bilateral chylothorax and association with chylous ascites have also been reported. Left-sided collections of lymph indicate an injury high in the duct.

In such thoracic operations as lobectomy, esophagectomy, rib resections for tumor or a Smithwick procedure, the position of the thoracic duct should be kept constantly in mind. Operations involving the left side of the lower part of the neck frequently endanger the thoracic duct.

The symptoms resulting from leakage of chyle are of two general types: those due to pressure and those due to loss of lymph chyle. If the duct is injured in the chest, pressure symptoms at first predominate, to be followed by the symptoms produced by the loss of large amounts of chyle. Dyspnea is usually the first indication that fluid is accumulating in the chest. This may be delayed twenty-four hours or several days, explainable on the basis of the fluid being first confined to the posterior mediastinum and later breaking through into the pleural cavity.

The continuous loss of chyle produces the symptoms expected from the escape of large quantities of fluid, rich in the same constituents as blood serum and, in addition, fat. Weakness, hunger and thirst develop. In a comparatively short time emaciation and inanition become striking features. There is a decrease in urinary output. The pulse becomes weak and rapid. Apathy supervenes, and death by starvation occurs in about three weeks.

Diagnosis may at first be confusing owing to a concomitant hemothorax. After repeated tapplings, the fluid clears and its true character can be recognized. It is milky in appearance and, on standing, separates into three layers: cream on the top; a second, milky, layer; and a lower layer, of cellular sediment. Lymph is alkaline in reaction and has a specific gravity of 1.012 or higher. Its white count may vary from 2,000 to 20,000 cells per cubic millimeter. Lymphocytes predominate, with a few eosinophiles, transitionals and unclassified cells. A few red cells are also usually present. As a result of the loss of lymphocytes in the chyle there is a drop in the lymphocyte count in the blood. Accompanying the large loss of chyle there is a general drop in the blood proteins and calcium.

#### REPORT OF A CASE

A patient, an army lieutenant, was received aboard a Navy hospital ship at Saipan, three days after being wounded. He was poorly oriented as to

time and place and in evident respiratory distress. The left side of the chest was splinted, and the patient was expectorating a dark, bloody sputum. While he had multiple superficial wounds, the essential wound had been caused by a bullet entering the left scapular area at the level of the third rib and leaving in the left supraclavicular area, 2 cm. from the midline and 1 cm. above the clavicle. These were reported to have been sucking wounds, and both had been sutured on the beach. Thoracentesis yielded from the left side of the chest 500 cc. of air and 650 cc. of blood. This was followed by pronounced improvement in respiration and pulse. Twenty-five thousand units of penicillin was instilled into the pleural cavity, and the administration of sulfathiazole was started by mouth. Plasma and fluids were given intravenously. The following morning, increasing respiratory embarrassment required another thoracentesis, at which time 950 cc. of bloody fluid was removed. Twice daily, taps were necessary to relieve the dyspnea.

By the fourth day after admission the fluid became a lighter red, and because of the line of flight of the bullet my colleagues and I became suspicious of chylothorax, with injury to the thoracic duct just above the clavicle. It was not until the fifth day that the true character of the fluid became apparent, as shown by its milky appearance and the presence of fat globules. Between 1,700 and 2,400 cc. of chylous fluid was removed daily. The patient was given at least 2 units of plasma daily, together with 2,000 cc. of 5 per cent dextrose and isotonic solution of sodium chloride and placed on a low fat, high protein diet. Despite this therapy his condition became progressively worse. He was listless and apathetic. His cheeks and eyeballs were sunken, and he had the general emaciated appearance of a starving person. It was decided that continued medical management would be fruitless and that operation offered the only chance for recovery.

#### Laboratory Work Before Operation

|              |                           |                     |
|--------------|---------------------------|---------------------|
| 7/9/44.....  | Red blood cells           | 5,080,000           |
|              | White blood cells         | 10,500              |
|              | Hemoglobin                | 75 per cent         |
|              | Hematocrit                | 46 per cent         |
|              | Proteins                  | 5.1 mg. per 100 cc. |
|              | Whole blood chlorides     | 445 mg. per 100 cc. |
|              | Blood cholesterol         | 235 mg. per 100 cc. |
|              | Nonprotein nitrogen       | 47 mg. per 100 cc.  |
|              | Clotting time             | 2½ minutes          |
|              | Bleeding time             | 3 minutes           |
|              | Urine                     | Negative            |
|              | Culture of thoracic fluid | Negative            |
| 7/10/44..... | Red blood cells           | 4,400,000           |
|              | White blood cells         | 14,000              |
|              | Hemoglobin                | 75 per cent         |

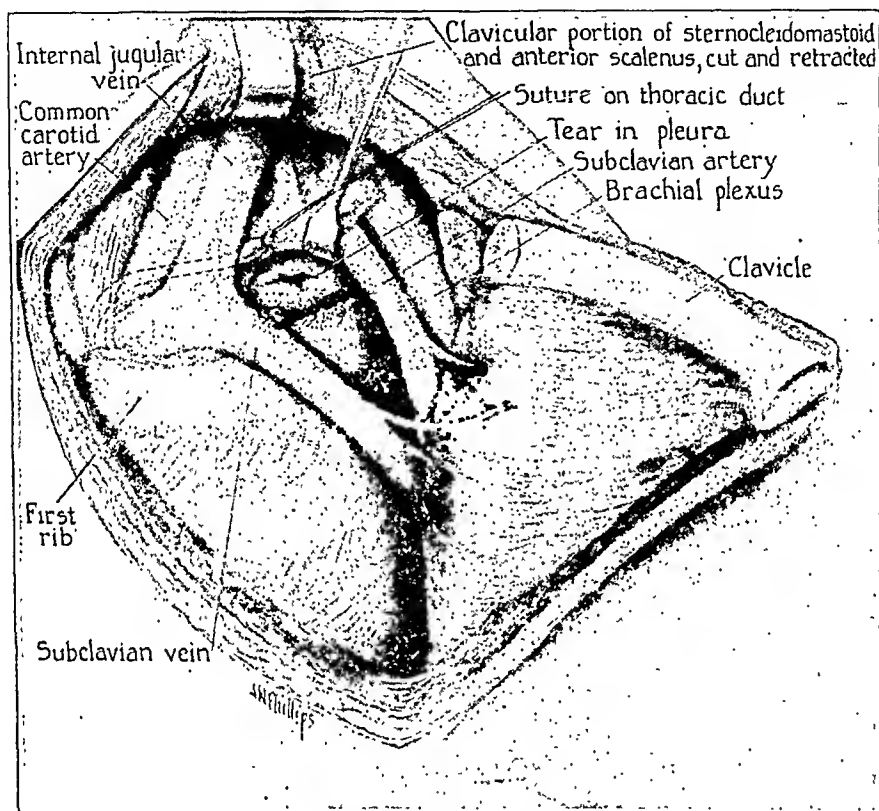
#### Laboratory Work After Operation

|                      |                   |             |
|----------------------|-------------------|-------------|
| 7/11/44.....         | Clotting time     | 3½ minutes  |
|                      | Bleeding time     | 3¾ minutes  |
| One month later..... | Serum protein     | 5.6 mg.     |
|                      | Hematocrit        | 36 per cent |
|                      | Red blood cells   | 4,490,000   |
|                      | White blood cells | 6,400       |
|                      | Hemoglobin        | 14.25 Gm.   |

His general condition was improved before operation by the administration of 2 units of plasma, 500 cc. of whole blood and 3,000 cc. of 5 per cent dextrose in isotonic solution of sodium chloride.

On July 10, 1944, nine days after admission, with the patient under anesthesia induced by ether administered intratracheally, an incision was made above and parallel to the clavicle. Considerable scar tissue from the trauma from the bullet was encountered. The thoracic duct could not be found, and it was decided to close the hole in the pleura, if this were possible. In order to obtain exposure,

a Sencert<sup>13</sup> type of incision was made. The clavicle was divided with a Gigli saw at the junction of the outer and middle thirds. The incision was swung around the sternoclavicular joint and downward and outward toward the anterior axillary fold. The pectoralis major and minor were detached from the chest, and the tissues swung outward with the outlined flap, after the sternoclavicular joint had been disarticulated. This gave excellent exposure to both the subclavian



Sencert's approach to the first and second portions of the subclavian vessels with the added step of severance of the anterior scalene muscle gave excellent exposure to the apex of the lung and the thoracic duct.

artery and the subclavian vein. After the anterior scalene muscle was divided, the perforation in the apical pleura, 1.5 cm. in diameter, became plainly visible. About 900 cc. of chyle was aspirated from the thoracic cavity, and the hole in the pleura was closed. That the bullet managed to pass between the subclavian artery and vein without damage to either will always remain an act of Providence. A final search for the thoracic duct in the neck revealed some slightly cloudy fluid seeping from behind the internal jugular vein. Elevation of the carotid sheath revealed the severed end, which was ligated with silk.

The following day the patient showed a remarkable change for the better. His former apathy had given way to an alertness that was obvious and a general

13. Bailey, H.: *Surgery of Modern Warfare*. Baltimore, William Wood & Company, 1941, vol. 1, pp. 299-300.



feeling of well-being. At 10 a.m. sudden dyspnea developed. A roentgenogram taken with a portable apparatus showed a 15 per cent pneumothorax on the right side, and several loculated pockets of fluid were seen on the left. Aspiration of air from the right side of the chest and fluid from the left side controlled his dyspnea, and improvement from then on was continuous. He was discharged to a base hospital on his fifth postoperative day, in good general condition.

A letter received from the subsequent medical officer in charge reported that one month after operation the patient was ambulatory and able to walk 200 yards (183 meters) without dyspnea; his total protein content was now 5.6 Gm. per hundred cubic centimeters; several taps had been necessary to remove small quantities of loculated fluid from the left side of the chest, and he had also recovered from pleurisy on the right side.

#### DISCUSSION OF THERAPY

It has been aptly shown that ligation of the thoracic duct in the neck can be done with impunity. If the duct is injured during operation, it is important to recognize it and to take the proper simple therapy of suture if the vessel is partially cut or ligature if it is severed. As the wall of the duct is thin and fragile and the pressure mounts considerably after ligation, added security may be obtained by burying the end into muscle or slipping it behind the sheath of a vessel—in the neck, the carotid sheath. Location of the duct may be a serious problem, and it is well to remember that it is most easily found behind the carotid sheath. A suggestion of Shackelford and Fisher, of giving a pint of cream one and one-half hours before operation to which has been added either scarlet red or sudan III, may be helpful.

Chylothorax due to intrathoracic injury offers a more difficult problem, because of the deep situation of the duct. The operative mortality has been reported as 100 per cent, but I have been able to find but 1 case in which ligation in the chest was performed. Whitcomb and Scoville<sup>14</sup> reported a recognized injury to the thoracic duct during a Smithwick operation for hypertension. Both ends of the duct were closed with double silver clips. Dyspnea from chylothorax developed on the seventh day probably due to erosion of the clips on the delicate wall of the duct. Death occurred suddenly, due to an anaphylactic reaction from intravenous administration of chyle. This case demonstrates the necessity of careful protection of the ligatured end of the duct.

In intrathoracic ductal injuries with chylothorax, conservative management has resulted in the appalling death rate of approximately 50 per cent. Conservative therapy consists in thoracentesis to relieve dyspnea, a high protein, low fat diet, intravenous administration of fluids and plasma, administration of amino acids and autogenous trans-

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14. Whitcomb, B. B., and Scoville, W. B.: Postoperative Chylothorax, *Arch. Surg.* 45:747 (Nov.) 1942.

fusions of chyle. Chyle, when proved sterile by culture, has been given both by direct and by indirect methods, with benefit. Because of the tremendous losses of fluid, dehydration has to be vigorously combated. In patients who recover under conservative management, the rent in the duct is undoubtedly healed over, much as a tear in a ureter.

It would seem logical to pursue conservative therapy for a reasonable period, in the hope of spontaneous closure, but with the patient's condition becoming worse surgical intervention would seem warranted.

The site for intervention is indicated by the side on which the chylothorax was located. In right-sided chylothorax, which predominates, the tear in the duct is usually just above the diaphragm, and a low transthoracic, right-sided approach is indicated. In left-sided chylothorax the tear in the duct is high, and the surgical approach has to be judged accordingly. Brown<sup>15</sup> described a posterior approach for lesions low on the right side, the object of which was to drain the chyle externally. It was undoubtedly hoped that the external fistula would close by contraction.

The difficulties of surgical intervention are appreciated, but they do not appear to be insurmountable and in the failing patient may reduce the extremely high mortality.

#### CONCLUSIONS AND SUMMARY

1. Chylothorax is a rare condition, 62 cases, including my case, having been reported up to the present time.

2. Injuries of the thoracic duct in the neck, either from accidents or during a surgical operation, are relatively common.

3. The continued loss of chyle results fatally, unless replaced.

4. Ligation of the thoracic duct, at least when injured in the neck, can be done without fear of disastrous results. Collateral circulation is adequate.

5. Chylothorax has had a 50 per cent mortality, and while conservative therapy may be pursued a reasonable length of time operation offers the best hope of reducing this figure.

6. A case of chylothorax, with successful outcome by ligation of the duct in the neck, is reported.

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15. Brown, A. L.: Traumatic Rupture of the Thoracic Duct with Bilateral Chylothorax and Chylous Ascites. *Arch. Surg.* **34**:120 (Jan.) 1937.

## ARTERIOSCLEROSIS OBLITERANS OF THE ABDOMINAL AORTA

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THE NUMBER of patients with slowly progressive thrombosis of the abdominal aorta has been small. In a review of the literature, Greenfield,<sup>1</sup> in 1943, stated that 161 cases of thrombosis and embolism had been reported. In 1940 Leriche<sup>2</sup> presented an excellent summary of the clinical course of progressive thrombosis of the abdominal aorta. On 4 patients he performed a bilateral lumbar sympathectomy, and in 1 patient he excised the lower portion of the abdominal aorta, removed the left lumbar chain and sectioned the right chain below the third lumbar ganglion.

Two patients were recently treated by me, and their cases are being presented in this paper. These cases are to be sharply differentiated from cases of acute embolic obstruction and rapidly progressive thrombosis of the aorta.

The development of the clinical syndrome into a recognizable pattern occurred over the course of three months. In both patients, a collateral circulation adequate to prevent necrosis developed through the upper lumbar, internal mammary and inferior mesenteric arteries. Symptoms appeared in direct relation to the ischemia of the lower extremities and in inverse proportion to the adequacy of the collateral supply. The 2 patients presented similar complaints and physical findings. An extreme fatigability of the lower extremities, intermittent claudication, coldness of the feet, atrophy of the calves and thighs and impotence were found in both men.

Examination revealed cool, pale feet, with few trophic changes in the skin, hair or nails. The pulsations of all major vessels in both lower extremities were absent. Pulsations of the abdominal aorta were easily palpable through the abdominal wall down to the level of the umbilicus but were absent from that point down. Pulsations of the inferior epigastric and circumflex iliac arteries were increased in

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From the Department of Surgery, Western Reserve University School of Medicine.

1. Greenfield, I.: Thrombosis and Embolism of the Abdominal Aorta, *Ann. Int. Med.* **19**:656 (Oct.) 1943.

2. Leriche, R.: Resection of the Iliac-Aortic Bifurcation with Bilateral Lumbar Sympathectomy, in Thrombosis of the Aorta, *Presse méd.* **48**:601 (July) 1940.

amplitude. The atrophy of the calves and thighs which had been noted by both patients was apparent on examination. The musculature was atonic. Deep reflexes were equal but diminished in intensity. Reflexes in the lower part of the abdomen and cremasteric and plantar reflexes were absent. Whether these alterations represent ischemia of the peripheral nerves or of the spinal cord because of thrombosis of the lumbar arteries is not clearly understood.



Fig. 1 (case J. C.).—Lateral roentgenogram of the lumbar portion of the spine, showing extensive calcification in the walls of the abdominal aorta and common iliac arteries.

Roentgenographic examination of the abdomen showed in both instances extensive calcification of the aorta in the lower part of the abdomen and the upper portion of both common iliac arteries (fig. 1). Roentgenograms of the extremities showed no calcification in the vessels. Oscillometric readings failed to demonstrate any pulsations in the thighs or calves. Dermathermic readings (fig. 2 A) showed significant elevations in the temperature of the feet following procaine hydrochloride block of the posterior tibial nerve.

Unaware of Leriche's paper at the time these 2 patients were seen, I thought that an interruption of the lumbar sympathetic nerves was indicated to promote as much collateral circulation as possible. This was performed through anterior Pearl<sup>3</sup> incisions. The immediate result was gratifying. Dermathermic readings (fig. 2 *B*) following the left lumbar sympathectomy showed adequate elevation of the temperature of the left foot in both patients. A long enough time has not elapsed to determine the end result of either the disease or the therapy.

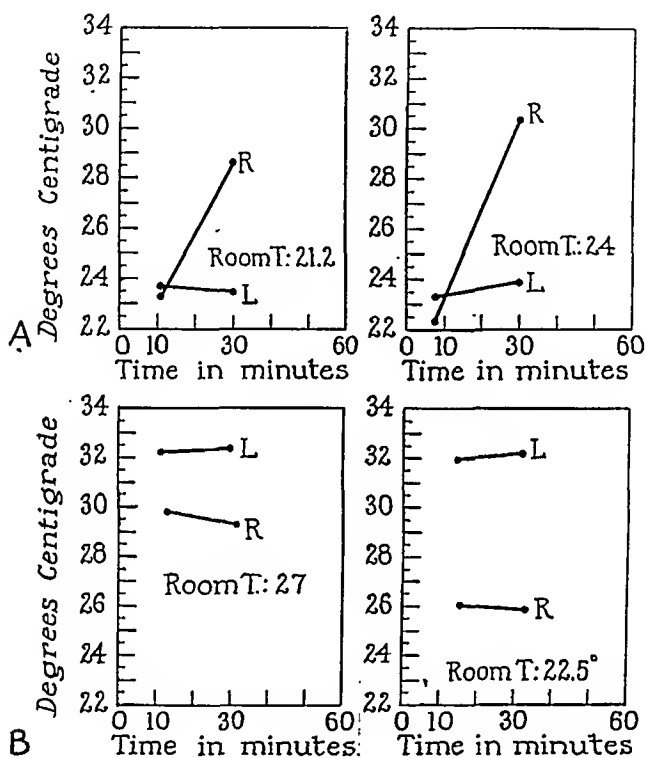


Fig. 2.—*A*, dermathermic readings of the right great toe following procaine hydrochloride block of the right posterior tibial nerve. *B*, dermathermic readings of the left great toe following left lumbar sympathectomy. (Left, case O. M.; right, case J. C.)

#### REPORT OF CASES

CASE 1 (referred by Dr. Harley Williams).—O. M., a 48 year old white man, six months previously had noticed numbness and tingling in the calves and feet after walking up two flights of stairs. During the following few weeks, these sensations arose after he went up short inclines. After he rested three to four seconds, the numbness disappeared. Three months before the admission of the patient to the hospital, the paresthesias were apparent after he had walked two blocks on level ground. At this time, he also observed that his feet felt cold

3. Pearl, F. L.: Muscle-Splitting Extraperitoneal Lumbar Ganglionectomy, Surg., Gynec. & Obst. 65:107 (July) 1937.

most of the time. During the month prior to admission the tingling had ascended to include the thighs, and at rest a burning pain was present on the lateral aspect of the thighs. He also stated that he had been impotent for several months. There was no disturbance of the upper extremities. The remaining history was irrelevant.

Examination revealed a tall, asthenic, intelligent man. All findings were within normal limits, except those stated in the following paragraphs. Neurologic investigation showed hyperesthesia on the lateral aspect of the left thigh. Deep reflexes were hypoactive, and superficial reflexes were absent. The muscles of the thighs and calves were flabby and atrophic. The pulsations of the aorta were easily palpable down to the level of the umbilicus. No pulsations were present in either lower extremity. The feet were cold and slightly moist to palpation. The color was pale. Venous filling time was twenty-seven seconds on the right and thirty-four seconds on the left.

The urine was straw colored, with a specific gravity of 1.009. There was no albumin or sugar, and the sediment contained an occasional leukocyte per high power field. The hemoglobin was 88 per cent, with a red cell count of 4,700,000. The white cell count was 4,300, with 60 per cent polymorphonuclears, 30 per cent lymphocytes, 8 per cent monocytes, and 2 per cent eosinophils. The serum calcium was 9.8 mg. per hundred cubic centimeters, phosphorus 4.2 mg. per hundred cubic centimeters, alkaline phosphatase 17.3 units, serum cholesterol 308 mg. per hundred cubic centimeters and cholesterol esters 201 mg. per hundred cubic centimeters.

Oscillometric readings showed no pulsations in either calf or thigh. Block of the right posterior tibial nerve with 1 per cent procaine hydrochloride showed a rise in the cutaneous temperature of the foot from 23.3 C. (73.9 F.) to 28.6 C. (83.4 F.). A roentgenogram of the abdomen and legs was reported: "There are linear streaks of calcification in the lower portion of the aorta. The calcification begins with the lower border of the third lumbar vertebra and can be traced as far as the lower border of the fifth lumbar vertebra. There is no other evidence of vascular calcification in the abdomen or legs."

A bilateral retroperitoneal lumbar sympathectomy, which included the excision of the second and third lumbar ganglions, was performed in two stages, without complication. Following the left lumbar sympathectomy, the temperature of the great toe (fig. 2 B) measured 32.3 C. (90.1 F.) compared with 29.8 C. (85.6 F.) on the side not operated on. Room temperature was 27 C. (80.6 F.).

One week following the operation, the patient was able to walk for twenty minutes without any pain in the lower extremities. He was readmitted to the hospital two months following the operation, because of a persisting hyperesthesia of the lateral femoral cutaneous nerve on the left side. This was relieved by injections of 1 per cent procaine hydrochloride into the lateral femoral cutaneous nerve and short wave diathermy to the lumbar area. He had had satisfactory sexual relations since discharge from the hospital.

CASE 2 (referred by Dr. Elton Recroft).—In J. C., a 46 year old white man, increasing intermittent claudication of both calves had developed six months previously. More pain was felt in the left than in the right calf. He observed that the left foot was colder than the right. Symptoms were more prominent in cold, wet weather. He had been impotent for several months. The patient had been receiving a deproteinized pancreatic extract, which had increased his tolerance to exercise more than twofold. The past-history revealed a fall on his back one

year prior to admission. This disabled him for only a few days. Five years ago, he was told that he had a calcium deficiency and was given 8 calcium tablets each day for three to four months. The dosage was not known. The remaining history was noncontributory.

Physical examination showed a well developed, well nourished, intelligent man appearing older than his stated age. The remainder of the examination showed no abnormalities except in the peripheral vascular and peripheral nervous systems. No pulsations of the aorta were present below the umbilicus, and no pulsations were palpable in any of the arteries of the lower extremities. Both feet were slightly cool. Venous filling time in the feet was thirty-five seconds and forty-two seconds on the right and left respectively. Deep reflexes in the lower extremities were hypoactive, and the musculature was atrophic.

The urine was clear, with a specific gravity of 1.001. There was no albumin or sugar, and the sediment contained 2 to 4 white blood cells per high power field. The hemoglobin was 110 per cent and the white cell count 7,150. The serum calcium was 10.7 mg. per hundred cubic centimeters, phosphorus 3.7 mg. per hundred cubic centimeters, alkaline phosphatase 5.2 units, serum cholesterol 207 mg. per hundred cubic centimeters and cholesterol esters 90 mg. per hundred cubic centimeters.

Oscillometric readings showed absence of pulsations in both lower extremities from the groin to the periphery. Following a posterior tibial block on the right with 1 per cent procaine hydrochloride, the temperature (fig. 2 *A*) of the great toe rose from 22.4 C. (72.3 F.) to 30.4 C. (86.7 F.), while the control remained at 23.9 C. (75.1 F.). The electrocardiogram was normal. Roentgenologic examination (fig. 1) showed severe calcific sclerosis of the abdominal aorta in front of the fourth and fifth lumbar vertebrae. There was no calcification in the vessels of the legs or feet.

A bilateral retroperitoneal sympathectomy was performed in two stages according to Pearl's technic. During the course of the left lumbar sympathectomy, the aorta was exposed. Pulsations were good down to 2 to 3 cm. above the bifurcation. Below this point, the aorta was about two-thirds its normal size, thickened and pulseless. The left common iliac artery also had no pulsations in the exposed 3 to 4 cm. The procedures were uncomplicated. The resting temperature of the great toes (fig. 2 *B*) rose to 32.1 C. (89.7 F.), and the extremities showed no sudomotor activity. Two months following the operation the patient's only complaint was mild aching in the thighs on arising in the morning. This disappeared during the day.

#### SUMMARY

Two cases of arteriosclerotic calcification and thrombosis of the abdominal aorta have been presented. The thrombosis occurred in men of 46 and 48 years. The relation of the autonomic nervous system to the collateral circulation and its interruption as a means of increasing that circulation is mentioned.

The incidence of this disease is probably much higher than is generally appreciated. The appearance of the extremities does not at first suggest arterial deficiency. The complaints referable to both lower extremities should lead to a careful examination of the peripheral pulses.

and abdominal aorta. The interpretation of the neurologic changes is difficult and will have to await microscopic examination of the spinal arteries, spinal cord and peripheral nerves. Oscillometric determinations and roentgenographic examination of the abdomen are helpful. The advisability of resecting the abdominal aorta as Leriche<sup>2</sup> reported should be considered in each individual patient. In general, however, to subject a patient to this procedure seems unwarranted, since the reaction itself should theoretically accomplish little in promoting collateral supply to the lower extremities.



# ACUTE FULMINATING ULCERATIVE COLITIS WITH MASSIVE PERFORATION AND PERITONITIS

Report of a Case

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THE RECENT opportunity to study in the ward and in the pathology laboratory a case of acute fulminating ulcerative colitis with massive perforation and peritonitis stimulated a review of the literature in this regard. Its rarity together with its urgent therapeutic demands prompts me to present the following study of a case with a review of the literature.

## REPORT OF A CASE

T. H. was a 43 year old, white woman, a divorcee, who was brought to the hospital in a state of profound shock. Her chief complaint was diarrhea of four weeks' duration. Because of her persistently critical condition and the absence of relatives, the history obtained is lacking in detail and probably to some extent in accuracy.

She was born in Oregon, had lived in the United States all her life and had come to Boston a few months previously. She had been married and divorced, was childless and had been employed as a millinery shop worker. Her health in the past had been good with a single exception. In California two years previously she had been hospitalized with postpneumonic empyema on the left side, drained by rib resection with subsequent thoracoplasty. Absolutely no significant history could be obtained of previous gastrointestinal disturbance, recent known exposure to enteric infection or food poisoning. There was no history of tuberculosis or contacts with tuberculosis.

*Present Illness.*—The immediate illness probably began about six weeks before entry, with stiffness and soreness of the muscles of the extremities and shoulder girdle. These symptoms were accompanied with slight malaise. There was no history of the patient's having ingested inadequately cooked pork or having had fever, alterations in bowel habits or abdominal cramps. She had felt well within a few days.

Four weeks prior to entry there was the insidious onset of moderately severe, crampy pain throughout the abdomen. Bowel movements occurred three times daily instead of once and afforded no relief from the abdominal distress. Stools were usually light yellow but occasionally black and always loose in consistency. The patient had never observed red blood in her stools prior to her entry into the hospital. Accompanying her diarrhea, anorexia began, which later became

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increasingly severe. There was no nausea, vomiting or localized pain. Three weeks before admission a low grade fever started. Abdominal pain became severer and was more pronounced on the left side. By ten days before entry, diarrhea, pain and weakness reached severe proportions and, in addition, the patient was persistently drowsy. During a single visit to her home, a local physician made a diagnosis of "intestinal influenza"; no chemotherapy or specific treatment was instituted. A Christian Science practitioner subsequently cared for the patient until her entry to the hospital. On the day of admission, she remembered only that the diarrhea was distinctly worse, with nearly continuous, watery, brownish yellow movements and generalized abdominal pains.

*Physical Examination on Entry.*—The temperature was 97.8 F., the pulse rate 120, the respiratory rate 36 and the blood pressure 85 systolic and 70 diastolic. She was critically ill, a fairly well preserved middle-aged woman in profound collapse. She seemed oriented but drowsy. She had no spontaneous pain. The extremities were cold, with a barely perceptible pulse at the wrist. The cheeks were sunken, but only slight generalized loss of weight was evident. The skin and mucous membranes were dry and generally pale, save for distinct reddening of the thenar and hypothenar eminences. No eruptions, petechiae or telangiectasia were observed. There was no local or general enlargement of the lymph nodes. The finger tips showed mild clubbing. The tongue was dry but not atrophic. The respiratory excursion was regular, rapid and shallow. In the lungs no abnormalities by percussion or auscultation were noted except for evidence of a thickened pleura at the left base, about the site of the old scar for empyema drainage. The heart seemed normal in size. The sounds were faint, and no murmurs could be detected. The peripheral veins were not visible, and on attempting to cut into the saphenous vein to give fluids we found that it was collapsed. The abdomen was distended, fairly tense and tympanitic. No mass or peristalsis was visible. There were diffuse generalized rebound and percussion tenderness and pain everywhere on pressure. No organs or masses were felt. No peristaltic sounds were audible. There was no evidence of a fluid wave. Pelvic examination revealed a rectovaginal fistula just inside the introitus, close to the posterior fourchet. There was moderate tenderness in the vaults, but no masses were felt. The rectal examination gave rise to considerable pain on pressure in all directions. No masses were noted. The neurologic findings were within normal limits.

*Laboratory Data.*—The hemoglobin content on entry was 7.8 Gm. It rose after repeated transfusions during the next three days to 12.2 Gm. The red cell count ranged from 2,900,000, on entry, to 4,280,000 after transfusion. The white blood cell counts ranged from 28,000, on admission, to 16,000, three days later. On smear there were many juvenile polymorphonuclear leukocytes, with a total count ranging from 92 to 95 per cent. No abnormal cells were seen.

Routine specimens of the urine concentrated to 1.022. No protein or sugar was present. Acetone was noted on entry, but none was subsequently found. Occasional red blood cells, white blood cells and hyaline casts were found in centrifuged sediment analyses.

The first stool examined after admission was brownish yellow and semiliquid and contained no blood according to the guaiac test. Subsequently, many stools were grossly bloody, with both bright red and changed blood. Smears of fecal material were negative for *Endamoeba histolytica*, *Balantidium coli* and *Mycobacterium tuberculosis*. Stool cultures were negative for pathogens; *Bacillus morgani* was obtained, but this did not agglutinate in anti-Shiga or in polyvalent antidyentery serums.

During life, blood was difficult to obtain and serologic tests of the blood, agglutination tests and culture studies were never done. Determinations of blood chemistry on heart blood immediately following death showed blood urea nitrogen 45 mg. per hundred cubic centimeters, nonprotein nitrogen 110 mg., total protein 6.5 Gm., albumin 3.6 Gm. and globulin 2.9 Gm.

*Hospital Course.*—After entry the patient's temperature fluctuated irregularly from 98.8 to 101.2 F. The pulse was always rapid, with an average reading around 115. Shortly after admission, the patient received 500 cc. of plasma, 1,000 cc. of compatible, cross-matched blood and 3,000 cc. of solutions containing sugar and isotonic solution of sodium chloride given intravenously. This resulted in considerable general improvement. Her blood pressure rose to 115 systolic and 75 diastolic, and concomitantly her heart sounds became readily audible, with a grade II preecordial systolic murmur. A roentgenogram of the chest showed only an elevated left diaphragm and a thickened pleura on that side, close to the site of the old rib resection. The heart and lungs appeared normal. Abdominal roentgenograms demonstrated moderate distention of the entire colon and blurring of the peritoneal lines. A roentgenogram of the abdomen with the patient in the erect position on the second day in the hospital showed no free air under the diaphragm.

Daily treatments included repeated attempts to pass a Miller-Abbott tube to relieve distention and the administration of plasma, blood and solutions containing salt and sugar.<sup>1</sup> Sodium sulfadiazine was given parenterally. Improvement continued for three days, with a slight drop in the pulse rate, stabilization of the blood pressure, clearing of the mental state and decrease in discomfort. There was no nausea or vomiting. The abdomen, however, remained unchanged, with distention, tenderness and absence of peristalsis. On the fourth hospital day the patient began to pass large amounts of bright red blood by rectum. Her blood pressure fell. She went into profound peripheral collapse, which was not remedied by repeated transfusions.<sup>1</sup> Rectal hemorrhage continued, and the patient died on the morning of the fifth day in the hospital.

1. Fluids administered were as follows:

|          |   |           |
|----------|---|-----------|
| 10/20/43 | Whole blood, 1,000 cc. given intravenously  |           |
|          | Plasma, 250 cc. given intravenously   |           |
|          | Plasma, 250 cc. given intrasternally  |           |
|          | 5 per cent dextrose in isotonic solution of sodium chloride, 2,000 cc. given intravenously  |           |
|          | 5 per cent dextrose in water, 1,000 cc. given intravenously                                 |           |
|          | 5 per cent dextrose in water, 1,000 cc. given by clysis                                     |           |
|          | Total   | 5,500 cc. |
| 10/21/43 | 5 per cent dextrose in isotonic solution of sodium chloride, 1,000 cc. given intravenously  |           |
|          | 5 per cent dextrose in isotonic solution of sodium chloride, 1,000 cc. given intrasternally |           |
|          | 5 per cent dextrose in water, 1,000 cc. given intrasternally                                |           |
|          | Total   | 3,000 cc. |
| 10/22/43 | 5 per cent dextrose in isotonic solution of sodium chloride, 1,000 cc. given intravenously  |           |
|          | 5 per cent dextrose in water, 1,000 cc. given intravenously                                 |           |
|          | Plasma, 250 cc. given intravenously   |           |
|          | Total   | 2,250 cc. |
| 10/23/43 | Whole blood, 1,000 cc. given intravenously  |           |
|          | Plasma, 500 cc. given intravenously   |           |
|          | 5 per cent dextrose in water, 1,000 cc. given intravenously                                 |           |
|          | 5 per cent dextrose in isotonic solution of sodium chloride, 1,000 cc. given by clysis      |           |
|          | Total   | 3,500 cc. |
| 10/24/43 | Plasma, 250 cc. given intravenously   |           |
|          | 5 per cent dextrose in isotonic solution of sodium chloride, 1,000 cc. given intravenously  |           |
|          | 5 per cent dextrose in water, 1,000 cc. given by clysis                                     |           |
|          | Total   | 2,250 cc. |

*Autopsy Report.*—On Oct. 25, 1943, ten hours after death, a complete necropsy was performed.

*Gross Pathology.*—Body: The body was well developed and well nourished, with an abundant amount of subcutaneous fat of normal distribution. The skin was ashen gray, finely textured and moderately dehydrated. The left side of the chest had a well healed, slightly depressed gray scar 10 cm. in length. On this side the thoracic wall was depressed and devoid of a normal bony cage over an area measuring 15 by 8 cm. Parts of the third, fourth, fifth and sixth ribs had been removed for local thoracoplasty after the patient's empyema was drained. Each rib lacked about 9 cm. of its total length.

The hair was finely textured, dark brown and of normal distribution. The eyeballs were unusually soft. The mucous membranes of the turbinates were crusted with dark brown material. The lips were dry, cracked and cyanotic.

The abdomen was ballooned out considerably, giving the appearance of an immense dome, whose apex was just below the navel. There were no dilated veins. The umbilicus was shallower and broader than usual. There was a fluid wave detectable in the flanks. The midabdomen anteriorly was tympanitic. The liver and spleen were not palpable. No other masses were made out, and no hernias were found.

The external genitalia were normally developed. Skene's and Bartholin's glands were not enlarged. The introitus admitted three fingers. The cervix was flat, firm and free of erosions. The perianal skin was excoriated. The mucocutaneous junction was prolapsed, 5 to 7 cm. being entirely visible. The rectal examination showed a small rectovaginal fistula, 2.5 cm. in diameter, 2 cm. inside the anal sphincter.

*Peritoneal Cavity:* When the abdominal cavity was opened, a large amount of gas escaped. Subsequently 2,100 cc. of chocolate brown, soupy fluid with a fecal odor was removed. This contained many free floating tabs of partially necrotized fatty tissue together with numerous droplets of liquid fat. The central portion of the omentum had several rents, where fat and its peritoneal covering had disappeared, leaving a skeleton of the larger vessels (fig. 1). Its right wing was attached to the anterior parietal peritoneum in the right lower quadrant; its left wing was attached to the upper sigmoid at the brim of the pelvis. Loculated, fecal-stained fluid was present in practically all recesses of the abdomen; 250 cc. was moved from the suprahepatic area, 250 cc. from the pelvis and 250 cc. from under the dome of the left diaphragm. Only the lesser peritoneal cavity was free of contamination; the foramen of Winslow was sealed off with fibrinous exudate.

The most striking feature was found in the large intestine. From the ileocecal valve to the rectosigmoid junction at the brim of the pelvis,

there was a continuous defect, involving all coats of the ventral (anti-mesenteric) side of the colon (fig. 1). The posterior half of the large intestine remained as an open trough in direct communication with the peritoneal cavity. This mucosa in some areas had been completely ulcerated away; in other areas irregular mucosal strands remained. The ulcerative process had burrowed deep into the submucosa, undermining cobweb-like shreds of mucosa. The result was a lacelike pattern covered with yellow fibrin on an irregularly burrowed and ulcerated submucosa and muscularis. No hemorrhages were noted. The entire large bowel



Fig. 1.—Diagrammatic illustration of massive ulceration of entire colon with destruction of antimesenteric border, with fenestration of the omental apron and with a large hydrosalpinx on the left side.

had previously been considerably dilated, because there was a pressure imprint on the inner surface of the anterior wall of the peritoneum.

In general the viscera were normal in size, shape and position. The liver was enlarged and extended down 6 cm. below the right costal margin in the midclavicular line. Its external surface was dark greenish brown, with some fibrin deposited on its peritoneal covering. The spleen was unusually small and flabby. The stomach had a hyperemic serosa with fibrinous exudate.

The small intestines were matted together with fibrinous exudate. Portions of the external surface of the small intestines which had come

into contact with the exposed posterior mucosa of the large intestines were eroded through the serosa and into the muscularis.

The pancreas was short but of usual breadth and depth. It was entirely enclosed in peripancreatic fat, the anterior portions of which appeared autolysed. The kidneys were not remarkable. In the pelvis the bladder was partially distended. The uterus was covered with fibrin.

To the right broad ligament was attached a small ovarian mass which was dark green, cystic, well encapsulated and 4.5 cm. in diameter. The left broad ligament was involved in an old inflammatory process involving the left tube, ovary, sigmoid and lateral uterine wall. The epiploic appendixes were adherent to the left tubo-ovarian inflammatory mass by dense fibrous adhesions.

**Pleural Cavities:** The right pleural cavity was normal except for a few fibrous adhesions on the posterior wall of the middle lobe. The left pleural cavity was obliterated by thick, dense, fibrous adhesions. These were most pronounced in the region of the rib resection and thoracoplasty. The anterior and superior aspects of both lungs were mottled pink and gray; the inferior and posterior surfaces were dark red and firm.

**Heart:** The heart weighed 300 Gm. This organ was essentially normal except for a shaggy, hard, wafer-shaped nodule about 4 mm. in diameter on one of the mitral cusps along the line of closure. There was no fresh friable thrombus. There was a firm annulus fibrosis. The myocardium and coronary vessels were not unusual.

**The Lungs:** The right lung weighed 420 Gm. and the left 280 Gm. Aside from the pleural adhesions already described, the only abnormality was an old, healed tuberculous nodule in the parenchyma of the left apex. The dark and firm character of the posterior and inferior aspects of both lungs was consistent with venous stasis. No pulmonary thrombi were found.

**Alimentary Tract:** The esophagus was normal. The stomach, duodenum, jejunum and ileum displayed fibrinous adhesions externally with irregular and scattered areas of serosal erosion previously mentioned. The mucosa was congested but free of hemorrhages, ulcerations and perforations.

After several days in 10 per cent solution of formaldehyde the sigmoid and rectum were opened. The same burrowing, necrotizing phlegmonous process was identified down to the mucocutaneous junction. No area of the large bowel was entirely free of the ulcerative process, although the midsigmoid was least affected. The ileocecal valve was opened from the proximal side. All the mucosa on the cecal side was involved in the inflammatory process, but the ileum was unaffected.

At the time of the gross autopsy the aorta was opened as well as the celiac axis, superior mesenteric artery and inferior mesenteric artery to their first bifurcations. No thrombi were observed. After fixation in solution of formaldehyde, dissection of these vessels to their attachments to the intestines was completed and no thrombi were observed.

**Pelvic Organs:** The bladder and uterus were not abnormal. The cystic tubo-ovarian mass on the right side was full of thick chocolate brown fluid. After fixation in 10 per cent solution of formaldehyde, the mass in the left broad ligament involving the sigmoid, uterus, ovary and tube was dissected. Another old scarred, walled-off, tubo-ovarian abscess was encountered, full of material similar to the one on the opposite side.

**Brain:** The weight of the brain was 1,340 Gm. There was no cerebral edema. No foci of hemorrhages, necrosis or thrombosis were found. After fixation in solution of formaldehyde, the brain was sectioned and the region of the thalamus and hypothalamus particularly carefully examined. No unusual observations were made.

**Spleen, Liver and Kidneys:** The spleen, liver and kidneys were not unusual.

*Microscopic Pathology.*—**Heart:** The suspected vegetation on the mitral valve showed only a local collection of hyaline material of fairly recent deposition. Otherwise the myocardium, endocardium and epicardium were not remarkable.

**Lungs:** Some congestion and patches of emphysema were the only abnormal findings.

**Pancreas:** No evidence of pancreatitis was found. There were patches of fibrosis and hyalinization at the expense of acinar tissue.

**Stomach and Small Intestine:** In several sections the serosa was involved in an acute inflammatory process, which occasionally extended into the outermost portions of the muscularis. The vessels were congested. The lymphatics were dilated. Large monocytes, plasma cells and large numbers of polymorphonuclear leukocytes had infiltrated the inflamed serosa. The mesothelial covering was discontinuous. The lining mucosa and submucosa were not abnormal.

**Large Intestine:** In all sections, observations corroborated the gross picture. In most areas the mucosa was completely ulcerated away (fig. 2). Where present, the muscularis mucosae was increased in prominence and thickness. Plasma cells and polymorphonuclear leukocytes had infiltrated all layers. A thick acidophilic membrane of fibrin and debris covered the ulcerated surfaces. The necrotizing process had extended into the submucosa and muscularis in many areas (fig. 3). Strands of coagulated fibrin separated submucosal hyaline connective tissue.

Lymphatics were dilated and full of granular debris. Blood vessels were surrounded by leukocytes; yet no evidence of a necrotizing arterioplitis was observed. In some zones even the muscularis had been destroyed. No inclusion bodies were observed. No amebas, trichinas, Balantidia or other parasites were found.

Spleen: The spleen displayed a mildly congested red pulp with scattered collections of polymorphonuclear leukocytes.



Fig. 2.—Microscopic view ( $\times 50$ ) of the rectal mucosa, showing the absence of the mucosa, erosion into the submucosa, congested vessels and dilated lymph vessels.

Liver: The liver was not abnormal.

Kidneys: In the kidneys, a few glomerular tufts contained fibrin thrombi but no congestion, inflammation or arteriolitis was observed. The tubules and renal pelvis were not unusual.

*Postmortem Bacteriology.*—Cultures of the heart blood yielded *Bacillus coli*, *Staphylococcus aureus* and *Staphylococcus albus*. Cultures



of the peritoneal fluid yielded *B. coli*, *Clostridium alcaligenes*, *Staph. aureus*, *Staph. albus* and an alpha hemolytic streptococcus. *Staph. aureus* colonies were coagulase negative. Swabs taken from the rectal mucosa and cultured according to Bargaen's technic failed to yield diplostreptococci.

*Summary of the Postmortem Findings.*—The body showed acute ulcerative colitis with extensive necrosis resulting in the disappearance



Fig. 3.—Microscopic view ( $\times 60$ ) of the cecal mucosa, showing discontinuity of the mucosa, erosion into the submucosa, congested vessels and dilated lymph vessels.

of the ventral (antimesenteric) half of the entire colon, from the ileocecal valve to the sigmoid. The remaining wall of the large bowel appeared as an open trough with severe cellulitis and erosion into the submucosa and muscularis. Accompanying this massive dissolution of the bowel wall was fecal peritonitis with 2,100 cc. of loculated purulent fluid. Anal excoriations and a rectovaginal fistula were noted. Incidental findings included a recent mitral valvular vegetation, old bilateral fibrous pleuritis, bilateral tubo-ovarian abscesses and atrophy of the pancreas.

## REVIEW OF THE LITERATURE

Most publications on ulcerative colitis are concerned with the chronic forms. In 1942, Brown, Buie and Weber<sup>2</sup> published an excellent classification of these conditions, largely based on endoscopic examinations. In 1943, Bargaen<sup>3</sup> published a monograph on "The Modern Management of Colitis," in which he classified colitis into nine separate groups; his is probably the best known and generally accepted classification. Under colitis he lists type I, tuberculous ulcerative colitis, caused by *Myco. tuberculosis*; type II, amebic ulcerative colitis, caused by *E. histolytica*; type III, bacillary dysentery, largely caused by several forms of organisms of the *Shigella paradysenteriae* group; type IV, thromboulcerative colitis, caused by the *Diplostreptococcus*<sup>4</sup>; type V, ulcerative colitis, caused by the virus of lymphogranuloma venereum; type VI, allergic colitis; type VII, colitis as part of the syndrome of dietary deficiencies; type VIII, chronic ulcerative colitis of unknown origin but definitely not caused by the *Diplostreptococcus*, and type IX, segmental ulcerative colitis, of unknown etiology. The last differs from type VIII only in distribution.

In all these conditions chronicity is outstanding except in a small group of cases under the classification of thromboulcerative colitis. Cases under this general classification Bargaen described as being "insidious," "severe" or "fulminating" in onset. Of 871 cases of thromboulcerative colitis which he studied at the Mayo Clinic, there were 163 cases of "fulminating" colitis; only 21 of these ended fatally. Little pathologic information is available concerning this group of patients. In a previous paper, in 1940, Schlicke and Bargaen<sup>5</sup> reported 20 cases of "fulminating" ulcerative colitis; in these only 3 patients had had symptoms of less than one year's duration. Nearly all exhibited an intermittent course, with chronicity as a prominent feature; acute ulcerations with perforations were merely terminal events. In all these reports it seems clear that these authors were dealing essentially with chronic colitis, a condition unlike that in the case under discussion. Furthermore, the *Diplostreptococcus* was recovered in 19 of the 20 cases of "fulminating" colitis reported by Schlicke and Bargaen but not in the present case.

2. Brown, P. W.; Buie, L. A., and Weber, H. M.: An Unclassified Type of Ulcerative Disease of the Colon, *South. M. J.* **35**:305, 1942.

3. Bargaen, J. A.: *The Modern Management of Colitis*, Springfield, Ill., Charles C Thomas, Publisher, 1943, p. 322.

4. The *Diplostreptococcus* is more commonly referred to in this condition as Bargaen's bacillus.

5. Schlicke, C. P., and Bargaen, J. A.: Fulminating Ulcerative Colitis: A Critical Analysis of Twenty Cases, *Minnesota Med.* **23**:348, 1940.

Since 1933 there have been 4 separate instances of simple acute ulcerative colitis among the Cabot case reports in the *New England Journal of Medicine*.<sup>6</sup> All the cases were without antecedent history of gastrointestinal disturbance, ran acute courses of less than nine weeks' duration and ended fatally, with perforation of the ulcerated colon and peritonitis. In 1937, Bunch<sup>7</sup> reported another acute case of phlegmonous ulcerative colitis with perforation and peritonitis; his patient died in a few days. In the discussion of Cabot Case 19,021,<sup>6a</sup> the late Dr. Daniel Jones stated that he had seen 2 or 3 similar patients, a few of which had recovered. He contended, together with Dr. Chester Jones, that this was a different entity from chronic ulcerative colitis with an acute "fulminating" terminal phase. Dr. Charles Lund<sup>6a</sup> is accredited with having saved a woman with a similar condition by doing an ileostomy and cutting the anal sphincter away from the infected colon for maximum drainage. The table summarizes the salient features of these 5 cases together with the present one.

From the table it is clear that in this group of cases age and sex are of no significance. All patients had diarrhea, some bloody, and others puriform and some with pain and 1 with no pain. The total duration of illness ranged from two days, in case 3, to nine weeks, in case 4. All had acute fulminating courses, with generalized peritonitis following perforation of the ulcerated colon. Five had a definite ulcerative process from the cecum to the rectum, and in only 1 was the process primarily confined to the descending colon. Five of the 6 patients were submitted to operation. Carefully selected surgical intervention in the case reported in this article might well have altered for the better the fatal course of the patient.

Although the laboratory studies are not complete in all 6 cases, it can be safely stated after a careful review of the available data that no known etiologic mechanism is detectable. Bargen was able to recover the *Diplostreptococcus* in most of his cases of acute "fulminating" ulcerative colitis. In at least 2 of these 6 cases this organism was sought but not recovered, despite the use of the technic recommended by

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6. (a) Acute Ulcerative Colitis with Perforation, Cabot Case 19021, *New Eng. J. Med.* **208**:89, 1933; (b) Acute Idiopathic Colitis with Perforation of Transverse Colon, Cabot Case 23201, *ibid.* **216**:894, 1937; (c) Ulcerative Colitis with Perforation of Cecum, Cabot Case 24041, *ibid.* **218**:183, 1938; (d) Acute Idiopathic Ulceration Colitis with Perforation, Cabot Case 27242, *ibid.* **224**:1029, 1941.

7. Bunch, G. H.: Acute Phlegmonous and Non-Traumatic Perforative Lesions of the Colon: Report of Three Cases with Intraperitoneal Hemorrhage Complicating One, *South. Surgeon* **6**:449, 1937.

*Salient Features of Five Cases From the Literature and Present Case*

| Case                            | Total Duration of Disease | Age, Sex Yr. | Chief Complaint                      | Operation   | Comment   | Pathologic Findings at Examination  |
|---------------------------------|---------------------------|--------------|--------------------------------------|---|---|---|
| 1. Cabot case 19021 (1933)..... | 6 weeks                   | F 22         | Diarrhea for 4 wk.                   | Exploratory laparotomy; ileostomy   | Diffuse peritonitis found at operation; died 18 hours after operation   | Ulceration of entire colon; perforation of sigmoid; generalized peritonitis                     |
| 2. Bunch (1937).....            | 3 days                    | M 35         | Abdominal pain and nausea for 48 hr. | Exploratory laparotomy; suturing of perforation   | Several inches of colon necrotic and perforated at operation; hemorrhaging from perforation; died 25 hours after operation  | Gangrene of descending colon; perforation; hemorrhage and peritonitis                           |
| 3. Cabot case 23201 (1937)..... | 2 days                    | M 60         | Abdominal pain for 1 day             | Exploratory laparotomy  | Diffuse phlegmon of colon found at operation  | Ulceration of entire colon; multiple perforations; generalized peritonitis                      |
| 4. Cabot case 24041 (1938)..... | 9 weeks                   | F 56         | Ischiorectal abscess for 3 weeks.    | 1. Incision and drainage of ischiorectal abscess; 2. Exploratory laparotomy drainage of abscess; Witzel enterostomy | Patient became distended and vomited after incision and drainage of abscess; abscess in right lower quadrant drained of laparotomy and ileostomy; died 3 days later | Ulceration of entire colon; perforation of cecum with abscess; generalized peritonitis          |
| 5. Cabot case 27242 (1941)..... | 8 weeks                   | F 39         | Bloody stools for 7 weeks.           | Cecostomy and appendicostomy  | Had had hemorrhoidectomy 2 weeks before entering Massachusetts General Hospital; died 3 days after cecostomy  | Ulceration of entire colon; perforation of sigmoid; generalized peritonitis                     |
| 6. Present case (1945).....     | 5 weeks                   | F 43         | Diarrhea for 4 wk.                   | None  | Patient improved for first 3 days in hospital; began hemorrhaging on 4th day; died on 5th day   | Ulceration of entire colon; perforation of colon from cecum to sigmoid; generalized peritonitis |

Bargen in 1935.<sup>8</sup> Mones and Sanjuan<sup>9</sup> expressed the opinion that a virus accompanying Bargen's diplostreptococcus was the causative agent in thromboulcerative colitis. In the study of the postmortem material in this case, inclusion bodies were carefully looked for but none were observed.

In 1940, Schlicke and Bargen<sup>10</sup> called attention to the fact that clubbed fingers occur oftener in conjunction with chronic ulcerative colitis than is generally appreciated. It is of interest to note that the case reported in this article is the only 1 of the 6 reviewed cases in which this condition was found. Whether this is an end result of the prolonged experience with pneumonia, empyema and thoracoplasty or with an unsuspected colonic lesion of long standing is a matter for conjecture.

#### CLINICAL COMMENT

The clinical diagnosis in cases of acute fulminating ulcerative colitis is probably best reached by exclusion. Tuberculous ulcerative colitis usually runs a chronic course, is oftener seated in the ileocecal region first and, by the time it involves the rectum, is frequently accompanied with multiple fistulas and sinuses. Pulmonary tuberculosis is commonly an accompaniment of tuberculous ulcerative colitis. Proctoscopic examination reveals irregularly shaped, shallow ulcers with yellow caseous bases often covered with a gray pellicle of fibrin. Recovery of *Myco. tuberculosis* from the stool is pathognomonic. Amebic dysentery is sometimes acute but oftener chronic in nature. On proctoscopic examination the ulcers are punched out and sharply delineated, with slightly elevated margins and grayish white fibrin caps over the bases. Identification of *E. histolytica* in stool preparations is diagnostic. Lymphogranuloma venereum occasionally runs a fulminating course with acute diarrhea. This occurs most frequently in Negroes. The Frei test is nearly always positive, although some patients acutely ill with lymphogranuloma have had repeatedly negative Frei tests until they began to improve. Bacillary dysentery due to *Bacillus typhosus*, *Bacillus paratyphosus*, *B. coli* and *Shigella dysenteriae* may run a severe fulminating course. Proctoscopic examination reveals no zone of the mucosa which is free of inflammation. The angry redness of pronounced hyperemia is striking. Petechial hemorrhages, shallow irregular ulcers

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8. Bargen, J. A.: *The Management of Colitis*, edited by M. Fishbein, National Medical Monograph, New York, National Medical Book Company, Inc., Doubleday, Doran & Company, Inc., 1935, p. 233.

9. Mones, F. G., and Sanjuan, P. D.: *Grave Ulcerative Colitis Without Amebic Etiology: Diagnosis with Lucid Treatment*, *Am. J. Digest. Dis. & Nutrition* 4:247, 1937.

10. Schlicke, C. P., and Bargen, J. A.: "Clubbed Fingers" and Ulcerative Colitis, *Am. J. Digest. Dis.* 7:17, 1940.

with angry red bases, edematous intervening mucosa—all contribute in making the diagnosis by direct visualization. Appropriate pathogenic organisms can be recovered by differential cultural methods. If the patients run a long enough clinical course, results of agglutination tests of the blood often become positive. Colitis due to *Ballantidium coli* may occur with acute diarrhea in any part of the world where hog meat is in the diet. Recovery of the large infusorian organisms from the stools is diagnostic. Diverticula of the large bowel with colitis are not uncommon. In this condition the illness usually occurs in an older age group and is customarily accompanied with premonitory signs and symptoms of rumbling abdominal cramps, intermittent bouts of diarrhea and localized abdominal tenderness. Later, chills and fever accompany severer diarrhea. These cases sometimes go on to intestinal obstruction when a palpable tender mass with local spasm is detectable. Carcinoma of the large intestine with ulceration, bleeding and diarrhea is also usually limited to an older age group and is accompanied with loss of weight and change in bowel habits running over a much longer period. Thromboulcerative colitis with severe diarrhea, variously termed idiopathic ulcerative colitis, colitis gravis and nonspecific ulcerative colitis, has an easily distinguishable proctoscopic picture which is fairly diagnostic. The mucosal lining is glazed, and over it are scattered multiple tiny gray granular dots, of less than a millimeter in diameter. When the mucosa is touched with an instrument, bleeding occurs readily. The lumen is narrowed, and the wall is diminished in flexibility. Tiny pocket-like scars are occasionally seen in cases of longer standing. This is the group of patients from whom Barger has been able to culture the diagnostic *Diplostreptococcus*.

The 6 cases of acute fulminating ulcerative colitis listed in table 1 do not correspond to any of Barger's types. In none is there a history of recent consumption of improperly cooked pork, exposure to tuberculosis or change in bowel habits. In only 1 instance was there a family history of ulcerative colitis; in that patient, whose brother had had the disease, there was history of loss of weight, overwork and emotional stress during the preceding year. In 1 other case the patient had vague rumbling left-sided abdominal cramps for several months before the onset of the immediate illness. The patients in the remaining 4 cases had explosive onsets of their intestinal disturbances. Unfortunately, because of the short duration and gravity of their illnesses, no proctoscopic findings were available.

Treatment of these patients was first supportive. They were given intravenous injections of dextrose and isotonic solution of sodium chloride, infusions of whole blood and plasma, sulfonamide drugs and chiniofon. To this armamentarium, penicillin now can be added. No

specific organisms were recovered in these cases ; had they been, vaccines may have been of some help. Five of the 6 patients were operated on. From a careful review of the 6 cases, it seems clear that well timed surgical intervention is probably of greatest benefit in this disorder. Once immediate supportive therapy has been instituted, an ileostomy is imperative to sidetrack the fecal stream. Moreover, in view of what Sweet has emphasized, i. e., that the colon in this condition can be excessively distended, cecostomy and/or appendicostomy together with pectinotomy of the anal sphincter are imperative to afford maximum decompression of and drainage from the affected colon.

#### SUMMARY

1. The clinical record and autopsy findings in a case of acute fulminating ulcerative colitis with peritonitis and extensive loss of bowel wall for its entire length are reported together with an analysis of similar records in the literature.
2. That this condition is probably different etiologically from the "fulminating" form of thromboulcerative colitis described by Bargen is emphasized.
3. The differential diagnosis in this condition is discussed.
4. Well timed surgical intervention in conjunction with general supportive therapy is stressed as the most valuable method of treatment.

# PRIMARY PERITONITIS CAUSED BY FRIEDLÄNDER'S BACILLUS

Report of a Case with Recovery Following Sulfadiazine Therapy

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AND

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FROM 1882, when Friedländer<sup>1</sup> described a micro-organism which he believed was the causative agent of lobar pneumonia, to recent times, infections with *Klebsiella pneumoniae* were thought to be almost wholly concerned with pathologic changes of the lungs. This concept of *Klebsiella* infection underwent a change following the report of Baehr, Shwartzman and Greenspan<sup>2</sup> in 1937. In a study of 198 cases of Friedländer's infections, these workers were able to establish a definite diagnosis of primary infection of the respiratory tract in only 2 cases. In approximately 80 per cent of their patients the primary sites of infection were the gastrointestinal tract, the genitourinary tract and the biliary passages and liver. So impressed were these investigators by the paucity of primary respiratory infections caused by this organism that they proposed a change of the name from *Klebsiella pneumoniae* to *Klebsiella friedländeri*. Since 1937 there have been a number of cases of extrapulmonary *Klebsiella* infections reported. However, in reviewing the literature, we are unable to find any previous report of primary peritonitis caused by *Klebsiella pneumoniae*. Because of the unusual clinical course of our patient, we believe that the case bears reporting.

## REPORT OF CASE

The patient, K. P., a 47 year old white man, a mechanic, was admitted to the Salt Lake County General Hospital on Nov. 6, 1945 at 6 p. m., with chief complaints of severe pain in the lower abdominal region, of five hours' duration, and nausea and vomiting for one day. Three weeks prior to admission he was affected with generalized abdominal discomfort, described as an ache with girdle distribution. The ache was constant, but the patient could obtain some relief by

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Miss Eleanor Willie conducted the bacteriologic studies.

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1. Friedländer, C.: Ueber die Schizomyceten bei der acuten fibrosen Pneumonie, *Virchows Arch. f. path. Anat.* **87**:319-324, 1882; *Die Mikrokokken der Pneumonie*; *Fortschr. d. Med.* **1**:715-733, 1883; *Weitere Bemerkungen über Pneumonia—Micrococcen*, *ibid.* **2**:333-336, 1884.

2. Baehr, G.; Shwartzman, G., and Greenspan, E. C.: *Bacillus Friedländer Infections*, *Ann. Int. Med.* **10**:1788-1801 (June) 1937.



lying very still. Although he said that there had been no febrility accompanied with chills, the patient stated the belief that for two or three nights immediately prior to admission he had had some fever. Morning vomiting, present occasionally for the past few years, was attributed to an "excess of phlegm." During the past year the patient had noted occasional night sweats. Because of the general abdominal discomfort, the patient had taken a liberal dose of a proprietary laxative, which had caused several loose bowel movements but had had no effect on his abdominal discomfort.

At 1 p. m. on November 6 the patient was sitting in his automobile when he was suddenly seized with sharp pain in the abdomen, which seemed to radiate from the right to the left lower quadrant and then to a lesser degree throughout the entire abdomen. The pain was of such intensity as to be almost intolerable. Nausea and vomiting accompanied the pain. Some measure of relief could be obtained by lying on his back with his legs drawn up, but this relief was not in any sense complete.

The past history revealed that the patient was treated at this hospital in 1937 for pneumococcic pneumonia, followed by empyema on the right side. The empyema was treated by rib resection and open drainage and resolved slowly over a period of three years. Since 1940 the sinus has been completely healed and symptomless except for occasional mild pain over the scar. A review of the systems revealed nothing of note except minimal dysuria with a little frequency and urgency of one month's duration. The family history was noncontributory.

Physical examination revealed a well developed, moderately obese white man in acute distress. The pulse rate was 92, blood pressure 130 systolic and 80 diastolic and oral temperature 101.6 F. There was minimal mucopurulent nasal discharge and slight pharyngeal injection. Examination of the chest showed dullness to percussion, diminished voice and breath sounds and tactile fremitus over the base of the right lung posteriorly. Breath sounds were vesicular in character. Both sides of the diaphragm descended well on inspiration. Many coarse, moist rales were heard posteriorly throughout both lung fields, which cleared when the patient was mobilized. There was an old, well healed scar in the right infra-scapular region, where the sinus tract had previously been. Moderate involuntary spasticity was present over the entire abdomen. Palpation revealed generalized abdominal tenderness, which was exquisite in the lower part of the abdomen, especially in the right lower quadrant. There was rebound tenderness referred to the right lower quadrant. No definite borborygmi were heard. It was impossible to feel the liver, kidneys, spleen or any mass. Old bilateral inguinal herniorrhaphy scars were noted. Generalized tenderness, more pronounced on the right side, was elicited on rectal examination. The prostate was essentially of normal size, shape and consistency and was not tender. Prior to operation the white blood cell count was 18,000, with a pronounced increase in the neutrophils, and the hemoglobin was 12.5 Gm. There were numerous white cells in the urine. The impression prior to operation was appendicitis, probably ruptured appendix, with abdominal abscess or spreading peritonitis.

*Operative Note* (Dr. P. B. Price).—A McBurney incision revealed diffuse inflammation of all the exposed peritoneal surfaces. A quantity of cloudy, odorless peritoneal fluid appeared, which was alkaline in reaction. The cecal wall and adjacent ileum were thick and edematous. A short, rudimentary appendix, lying retroperitoneally in a posterior position, was removed, although it appeared grossly to be uninvolved in the inflammatory process. Subsequent histologic examination confirmed that impression. The abdominal incision was then extended medially to permit a more satisfactory search for the source of the infection. Turgid, acutely

inflamed coils of small intestine were encountered, which were matted together with fibrin, pocketing off collections of thin yellowish pus. The mesentery in particular was thick with edema and acute inflammatory reaction. There was no evidence of diverticulitis, perforation or intestinal obstruction. Cautious palpation showed that the upper part of the abdomen was less seriously involved in the inflammatory process than the lower part. The operator's opinion at this time was that the patient had primary peritonitis. Since the condition of the patient did not appear to justify further exploration, the incision was closed without drainage.

The results of the various specimens cultured are shown in the table. *Klebsiella* organisms from both the peritoneal exudate and the cultures of material from the throat showed the characteristic quellung reaction when mixed with *Klebsiella* type A antiserum. Antibiotic tests in vitro using a synthetic medium showed *Klebsiella* organisms completely inhibited by sulfadiazine at a concentration of 3 mg. Penicillin had no inhibitory effect at concentrations of 0.13 units to 5 units

### *Bacteriologic Studies*

| Date    | Specimen             | Culture  | White Blood Cell Count |
|---------|----------------------|--|------------------------|
| 11/6/45 | Peritoneal exudate   | Numerous <i>Klebsiella pneumoniae</i><br>Few <i>B. hemolytic anaerobic streptococci</i>        | 18,000                 |
| 11/10   | Blood                | Sterile  | 19,000                 |
|         | Material from throat | <i>Klebsiella pneumoniae</i>   |                        |
| 11/11   | Urine                | Sterile  | 12,500                 |
|         | Blood                | Sterile  |                        |
|         | Feces                | Negative for <i>Klebsiella</i> organisms<br>and other pathogens                                |                        |
| 11/12   | Incision drainage    | <i>Klebsiella</i> organisms<br>Few diphtheroids<br>Few gram-positive rods<br>Few staphylococci | 12,500                 |
| 11/14   | Incision drainage    | Few <i>Klebsiella</i> organisms  | 13,000                 |
| 11/15   | Material from throat | Negative for <i>Klebsiella</i> organisms   | 12,500                 |
|         | Stool                | Negative for <i>Klebsiella</i> organisms   |                        |
| 11/17   | Material from throat | Negative for <i>Klebsiella</i> organisms   | 13,000                 |
| 11/26   | Urine                | Enterococci  | 11,000                 |
| 11/27   | Material from throat | Negative for <i>Klebsiella</i> organisms   | 10,000                 |

per 0.5 cc. Results of urinary examinations were essentially normal with the exception of the first specimen, which showed numerous white blood cells. The Mantoux test elicited a negative reaction, and examination of a three day specimen of sputum revealed no acid-fast bacilli.

Intraperitoneal injection into 2 mice, cultures of material from the throat into 1 and cultures of material from the peritoneum into 1, resulted in fulminating *Klebsiella* infections which killed the mice in seventeen and twenty hours. Intracardiac injection of a culture into a guinea pig resulted in death in twenty-four hours from *Klebsiella* septicemia, peritonitis and meningitis.

The course of the patient was remarkably smooth. His temperature rose to 99.8 F. each afternoon until one week postoperatively, at which time his incision was opened at either end to establish free drainage. Following this the wound healed rapidly and cleanly.

At this time the patient presented signs and symptoms of a mild coryza, which disappeared three days later. Subjectively, he offered no complaints subsequent to the first week in the hospital. Postoperative therapy consisted in simultaneous administration of sulfadiazine and penicillin until the nature of the

infection was determined; penicillin was then discontinued because in vitro studies showed the organism to be inhibited by sulfadiazine but not by penicillin. The patient continued to improve and was discharged as cured on the twenty-sixth hospital day.

#### COMMENT

Although the impression of primary peritonitis was gained during the operation, the diagnosis was not considered to be reasonably established until corroborative bacteriologic studies had been made and additional studies failed to reveal other sites of pathologic changes caused by *Klebsiella* organisms. The primary sites of *Klebsiella* infection to be considered would be the following: the gastrointestinal tract, the biliary passages and the liver, the genitourinary tract and the lungs and upper respiratory tract. A brief consideration of each of these possible sources shows that the probability of this clinical picture originating from any of these sites on the basis of antecedent infection is remote.

*Gastrointestinal Tract.*—The means by which a *Klebsiella* infection could conceivably originate from this site would be (a) a perforative lesion of the stomach, appendix or small or large bowel, (b) an intra-abdominal abscess, periappendicular or otherwise, and (c), questionably, inflammation of the gastrointestinal tract. These possibilities were ruled out in the following manner: (1) normal operative conditions; (2) two successive stool cultures negative for *Klebsiella* organisms or other pathogens; (3) absence of the usual intestinal flora and feculent odor in the peritoneal exudate; (4) normal postoperative roentgenologic and fluoroscopic examinations of the entire gastrointestinal tract, and (5) the remarkably smooth postoperative course, which strongly suggests that no large degree of pathologic change in the bowel was present.

*Biliary Passages and Liver.*—When this part of the anatomy is infected with *Klebsiella* organisms, certain signs and symptoms are almost invariably noted. Stasis in the biliary tract plays an important role in predisposing to infection at this site. Boettiger<sup>3</sup> in reporting 2 cases of hepatic abscesses due to *Klebsiella* organisms pointed to the extreme rarity of this condition (25 reported cases since 1900), the septic course and the fact that conditions reported as primary hepatic abscesses are more likely secondary to intestinal or biliary infection. Perforation of the gallbladder is another possible source of peritonitis. According to Baehr and co-workers<sup>2</sup> more than 80 per cent (38 of 46 cases) of patients with *Klebsiella* infection of the biliary passages have demonstrable cholelithiasis. We believe that this potential source of infection may be eliminated in our case by the following facts:

3. Boettiger, C.; Weinstein, M., and Werne, J.: Primary Suppuration of Liver Due to Friedländer's Bacillus, *J. A. M. A.* **114**:1050-1055 (March 23) 1940.

(1) no symptoms of biliary obstruction noted in the history; (2) absence of septicemic history and absence of signs of septicemia during hospitalization; (3) no signs of tenderness in the right upper quadrant or hepatic enlargement at any time before or following operation; (4) postoperatively a normal functioning gallbladder and the absence of any cholelithiasis or common duct obstruction as evidenced by the Graham-Cole test; (5) absence of bile in the peritoneal exudate, and (6) the remarkably benign postoperative course.

*Genitourinary Tract.*—Reports of prostatic<sup>4</sup> and perirenal<sup>5</sup> abscesses caused by Klebsiella organisms have appeared in recent years. It is important to note that Klebsiella infections of the urinary tract are often associated with other organisms, viz., *Escherichia coli*, *Bacillus pyocyaneus*, and *Proteus vulgaris*. As with biliary infections, so here, stasis is apt to be encountered, with resultant kidney infection. In our opinion Klebsiella infection of the genitourinary tract is inconsistent with the clinical findings in our case for the following reasons: (1) absence of Klebsiella organisms in the urine on repeated cultures (absence also of *E. coli*, *B. pyocyaneus* and *P. vulgaris*); (2) normal urinary conditions with the exception of initial, mild pyuria; (3) normal excretory urograms; (4) normal psoas shadows and kidney outlines on the roentgenograms; (5) no tenderness in the costovertebral angle elicited at any time, and (6) normal prostate on digital examination.

*Lungs and Upper Respiratory Tract.*—In addition to acute Friedländer's pneumonia, chronic Friedländer infections of the lungs, nose and sinuses, ears and pharynx have been described. Because of the history of previous pneumonia complicated by long-standing empyema and because of the positive culture of material from the throat obtained four days after admission to the hospital, our main interest centered here as a likely primary source of the infection.

In view of the patient's history, it would seem unnecessary to discuss any of the aforementioned conditions except chronic Friedländer infection of the pharynx and of the lungs. Chronic Friedländer infection of the lungs, as reported by Solomon,<sup>6</sup> is a proved, although probably not generally recognized, disease which could conceivably give rise to a picture of this type. The history of morning cough, "excess of phlegm" and occasional night sweats at once suggested that

4. Pfeiffer, D. B.: Klebsiella Pneumoniae Bacteremia Due to Prostatic Abscess: Case with Recovery, *Ann. Surg.* **106**:1115-1118 (Dec.) 1937.

5. Kindall, L.: Perirenal Abscess with Gas Formation and Metastatic Pulmonary Abscesses Due to Friedländer's Bacillus: Case Report, *J. Urol.* **46**:555-561 (Sept.) 1941.

6. Solomon, S.: Chronic Friedländer Infections of Lungs: Report of Seventeen Cases and Observations on Therapy with Sulfapyridine and Sulfanilamide, *J. A. M. A.* **115**:1527-1536 (Nov. 2) 1940.

Klebsiella organisms might be culpable as an etiologic factor. In the 17 cases studied by Solomon, almost constant symptoms and signs were pleurisy, hemoptysis, chills and fever at the onset and complications consisting mainly of pulmonary abscess, empyema, pleural effusion and, less frequently, pulmonary fibrosis. Our reasons for rejecting the previously mentioned sites, with the exception of the pharynx, are as follows: (1) absence of pleurisy, hemoptysis, chills and fever since the patient's recovery from pneumococcic pneumonia and empyema eight years ago; (2) absence of history and physical findings of the previously listed complications; (3) normal chest on roentgenologic examination except for pleural thickening at the base of the right lung and (4) absence of antibodies (agglutinins or capsule-swelling antibodies) in the patient's serum for four weeks after admission.

Although Klebsiella organisms were cultured from the pharynx four days after admission, the patient at no time had signs or symptoms of clinical pharyngitis. It should be noted that the organisms were discovered there unexpectedly on routine cultures to determine a possible source of infection. Routine cultures of material from the throat show that approximately 5 per cent of the population harbor Klebsiella organisms.<sup>7</sup> It is possible that the pharynx was the portal of entry of the organism in our patient and that spread was by way of the blood stream to the peritoneum.

#### SUMMARY

1. A case of a condition believed to be primary peritonitis caused by *Bacillus friedländeri* is presented.

2. Under sulfadiazine therapy the patient made a remarkably rapid and smooth recovery.

3. As far as we can determine, this is the first case of primary peritonitis of this sort to be reported.

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7. Bloomfield, A. L.: The Mechanism of the Bacillus Carrier State with Special Reference to the Friedländer Bacillus, *Am. Rev. Tuberc.* 4:847 (Jan.) 1921.

## BLOOD LEVEL OF PHENOL IN UREMIA

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FISHBERG<sup>1</sup> has defined uremia as "A complex auto-intoxication, the variegated clinical picture being the summation of the effects of retention of various urinary constituents." He showed that virtually every known urinary constituent has at one time or another been indicted as an etiologic factor in the production of this syndrome. Of the various retained excretory products, certain ones seem to play a primary role while others are entirely of secondary importance. Some of the manifestations of the uremic syndrome are as yet unexplained, among them various types of cutaneous lesions, pericarditis and others. However, through extensive investigations in recent years, an approach to the more important manifestations has been gained.

Raab<sup>2</sup> has postulated that the presence of catechol and phenol compounds is a highly contributory if not the main cause of the electrocardiographic changes and the physical signs of cardiac failure in uremic patients.

The gastrointestinal symptoms have been attributed by Mason and his associates<sup>3</sup> to: (1) the retention of urea, which (a) forms ammonium salts by bacterial decomposition in the alimentary tract and (b) prevents the disposition of guanidine; (2) guanidine intoxication, which in itself produces gastroenteritis, and (3) dehydration and acid-base imbalance, which are thought to be of secondary importance and are occasionally absent.

Respiratory symptoms have also been ascribed to retention of guanidine<sup>3</sup> and to acidosis.

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From the Departments of Urology and Biochemistry, University of Michigan Medical School.

1. Fishberg, A. M.: *Hypertension and Nephritis*, ed. 4, Philadelphia, Lea & Febiger, 1940.

2. Raab, W.: *Cardiotoxic Substances in the Blood and Heart Muscle in Uremia*, *J. Lab. & Clin. Med.* **29**:715-734 (July) 1944.

3. Mason, M. F.; Resnik, H.; Minot, A. S.; Rainey, J.; Pilcher, C., and Harrison, T. R.: *Mechanism of Experimental Uremia*, *Arch. Int. Med.* **60**: 312-336 (Aug.) 1937.

Of the greatest interest have been the nervous manifestations of uremia. Mason and his co-workers<sup>3</sup> have expressed the opinion that uremic patients are "subjected to two major antagonistic influences—stimulation and depression." A deficit in the calcium ion concentration in the cerebrospinal fluid produces symptoms of irritation (restlessness, muscular twitchings, convulsions and similar signs). A deficit in calcium ions results primarily from phosphate retention. On the other hand, elevated cerebrospinal phenol has a narcotic effect which is productive of somnolence, apathy, disorientation and coma. According to Fishberg,<sup>1</sup> Becher has shown that the latter symptoms do not appear until the phenol enters the cerebrospinal fluid. Also complicating this "balance" is the retention of guanidine,<sup>2</sup> which can produce either irritative or depressive symptoms, depending on the level, on whether or not a central deficit of calcium ions exists and on other factors.

Needless to say that from these studies the postulate of a unitary basis of uremia has long been discarded. As mentioned previously, several investigators have shown conclusively that "phenol" is elevated in uremia. However, Roen<sup>4</sup> has pointed out that their tests of phenol were nonspecific, measuring not only phenol but "also such substances carrying the phenol grouping and its various substitutions as phenol itself, p-cresol, diphenol, indican, skatol, indole, and other related compounds."

Roen,<sup>4</sup> in his investigation of 30 uremic patients at the Cleveland Clinics, employed a new method of determining the level of phenol in blood, which was devised by Bernhart. By this method the reaction is highly specific for the phenol structure and there is only a 3 per cent technical error. From his studies he has concluded the following:

The phenol level in blood is increased in renal failure accompanied by uremia.

The blood phenol is elevated in all cases of uremia regardless of the type of renal failure.

The blood phenol is not elevated in simple blood nitrogen retention where there are no uremic symptoms.

The height of the blood phenol, though generally related to the uremic symptoms, is not in direct proportion to the intensity of the uremic state

The methods employed in our studies have been identical with those of Roen, since we have endeavored to substantiate the evidence he presented. Table 1 is a series of normal values determined on the blood of normal persons. These values give us a basis for considering 2.0 mg. per hundred cubic centimeters as the upper limit of normal for the level of phenol in the blood. Our method of determining the level of

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4. Roen, P. R.: The Chemical Basis of Uremia: Blood Phenol, *J. Urol.* 51:110-116 (Jan.) 1944.

urea in the blood is that of Barker.<sup>5</sup> The normal value varies between .10 and 20 mg. per hundred cubic centimeters. Normal values of urea in the blood appear in table 2.

In addition to the lists of normal values in tables 1 and 2, we have studied a small series of patients in whom there were no uremic symp-

TABLE 1.—*Normal Values for Phenol in Blood of Normal Persons*

| Subject | Mg./100 cc. | Mg./100 cc.<br>Added | Mg./100 cc.<br>Recovery | Per Cent<br>Recovery |
|---------|-------------|----------------------|-------------------------|----------------------|
| C.....  | 0.50        | 1.50                 | 1.50                    | 100                  |
| Ki..... | 1.30        | 1.60                 | 1.70                    | 106                  |
| E.....  | 1.80        | 0.75                 | 0.70                    | 93                   |
| R.....  | 0.70        | 2.50                 | 2.50                    | 100                  |
| D.....  | 1.15        | ....                 | ....                    | ...                  |
| G.....  | 1.00        | ....                 | ....                    | ...                  |
| K.....  | 0.60        | ....                 | ....                    | ...                  |
| O.....  | 1.10        | ....                 | ....                    | ...                  |

TABLE 2.—*Normal Values for Urea in Blood of Normal Persons*

| Subject | Mg./100 cc. | Mg./100 cc.<br>Added | Mg./100 cc.<br>Recovery | Per Cent<br>Recovery |
|---------|-------------|----------------------|-------------------------|----------------------|
| A.....  | 12.5        | 12.5                 | 13.5                    | 108                  |
| B.....  | 15.0        | 25.0                 | 27.0                    | 108                  |
| G.....  | 16.2        | ....                 | ....                    | ...                  |
| K.....  | 18.8        | ....                 | ....                    | ...                  |
| O.....  | 15.0        | 27.5                 | 27.0                    | 98                   |
| M.....  | ....        | 50.0                 | 48.0                    | 96                   |
|         | ....        | 75.0                 | 73.0                    | 97                   |
| C.....  | 12.0        | 25.0                 | 25.5                    | 102                  |
| Ki..... | 18.0        | 50.0                 | 51.0                    | 102                  |
| E.....  | 13.0        | ....                 | ....                    | ...                  |
| R.....  | 16.0        | ....                 | ....                    | ...                  |

TABLE 3.—*Values for Urea and Phenol in Cases of Patients Without Uremic Symptoms*

| Case | Diagnosis                             | Urea  | Uremic<br>Symptoms | Phenol |
|------|---------------------------------------|-------|--------------------|--------|
| 1    | Pernicious anemia .....               | 9.25  | 0                  | 1.75   |
| 2    | Normochromic anemia .....             | 22.50 | 0                  | 1.80   |
| 3    | Aleukemic myeloblastic leukemia ..... | 10.0  | 0                  | 1.08   |
| 4    | Hodgkin's disease .....               | 9.0   | 0                  | 1.20   |
| 5    | Hodgkin's disease .....               | 9.5   | 0                  | 1.80   |
| 6    | Chronic myelogenous leukemia .....    | 18.0  | 0                  | 1.55   |
| 7    | Lymphogenous leukemia .....           | 28.0  | 0                  | 1.14   |

toms and in whom renal pathologic changes were not a factor. Their cases, then, also constitute a table of normal values.

5. Barker, S. B.: The Direct Colorimetric Determination of Urea in Blood and Urine, J. Biol. Chem. **152**:453-463 (Feb.) 1944.



After the manner of Roen we have divided our patients into several categories according to the types of renal dysfunction. Since our interest has been primarily concerned with urologic problems, the majority of our patients are those suffering from various types of obstructive uropathy. Table 4 shows a series of 20 cases of postrenal obstructive uropathy.

TABLE 4.—*Values for Urea and Phenol in Cases of Postrenal Obstructive Uropathy*

| Case | Date    | Diagnosis   | Urea | Uremic Symptoms | Phenol |
|------|---------|---|------|-----------------|--------|
| 8    | 6/19/44 | Benign prostatic hypertrophy; overflow incontinence .....   | 62   | ++              | 2.18   |
| 9    | 7/24/44 | Carcinoma of the urethra; complete retention..  | 58   | ++++            | 3.20   |
| 10   | 1/20/45 | Carcinoma of the bladder, with ureteral obstruction .....   | 158  | ++++            | 5.10   |
| 11   | 6/14/44 | Carcinoma of the prostate .....   | 134  | +++             | 2.85   |
| 12   | 6/13/44 | Metastatic carcinoma of the rectum; ureteral obstruction .....  | 64   | ++++            | 2.25   |
| 13   | 6/15/44 | Benign prostatic hypertrophy; complete retention .....  | 154  | +++             | 10.80  |
| 14   | 2/13/44 | Carcinoma of the prostate; complete retention .....   | 33   | +++             | 2.40   |
| 15   | 6/22/44 | Benign prostatic hypertrophy .....  | 51   | +++             | 2.04   |
| 16   | 6/23/44 | Carcinoma of the prostate; extension to ureters .....   | 132  | ++              | 2.93   |
| 17   | 8/ 4/44 | Benign prostatic hypertrophy; complete retention .....  | 95   | ++++            | 7.20   |
| 18   | 7/ 3/44 | Carcinoma of the prostate .....   | 75   | 0               | 2.40   |
| 19   | 1/30/45 | Benign prostatic hypertrophy; 10 days after cystostomy .....  | 75.5 | +               | 1.40   |
| 20   | 6/15/44 | Benign prostatic hypertrophy; complete retention; 2 days after transurethral resection .....                          | 28   | 0               | 4.0    |
| 21   | 6/19/44 | Benign prostatic hypertrophy; 7 months after cystostomy and 9 days after transurethral resection .....                | 64   | 0               | 2.40   |
| 22   | 7/ 5/44 | Vesical neck contracture after sodium chloride administered orally and sodium bicarbonate....                         | 60   | 0               | 2.20   |
| 23   | 6/14/44 | 2 yr. after cystectomy and bilateral cutaneous ureterostomy .....   | 146  | 0               | 5.42   |
| 24   | 8/15/44 | Benign prostatic hypertrophy, with overflow incontinence .....  | 19   | 0               | 2.46   |
| 25   | 1/30/45 | Benign prostatic hypertrophy; obstructive uropathy; postcatheter drainage and fluids administered intravenously ..... | 60   | 0               | 1.41   |
| 26   | 7/ 5/44 | Benign prostatic hypertrophy .....  | 18   | 0               | 1.70   |
| 27   | 8/11/44 | Benign prostatic hypertrophy; vesical calculus..  | 29   | 0               | 1.65   |

From the values given in table 4, several broad generalities may be made:

1. In the majority but not all of the cases of postrenal obstructive uropathy with nitrogen retention, the level of phenol in the blood is elevated.

2. Uremic symptoms, while frequently present, are not always related to an elevated level of phenol. This applies not only to uremic symptoms in general but especially to symptoms of narcosis:

3. No parallelism occurs between the intensity of the uremic symptoms and the blood level of phenol.

4. There is no proportionate correlation between the blood levels of urea and phenol.

While our series of primary renal disease is small (table 5), the preceding conclusions apply in this type of pathologic changes too.

Only 1 case of prerenal azotemia was studied. The patient was a 49 year old man with traumatic rupture of the right kidney. Urinary output was exceeding 2,000 cc. per twenty-four hours at the time the determinations of blood chemistry were made. The value for urea was

TABLE 5.—*Values for Urea and Phenol in Patients with Primary Renal Disease*

| Case | Date    | Diagnosis                               | Urea | Uremic Symptoms | Phenol |
|------|---------|---|------|-----------------|--------|
| 28   | 1/11/45 | Chronic nephritis, hypertension .....   | 46   | 0               | 2.15   |
| 29   | 8/11/44 | Malignant hypertension .....            | 73   | ++++            | 1.62   |
| 30   | 1/10/45 | ? Acute hemorrhagic nephritis .....     | 38   | ++              | 1.90   |
| 31   | 6/26/44 | Chronic active glomerulonephritis ..... | 88   | +               | 3.12   |
| 32   | 7/21/44 | Chronic active glomerulonephritis ..... | 132  | +               | 1.85   |

TABLE 6.—*Level of Phenol in Blood of Patients Who Died*

| Case | Date         | Days Before Death | Phenol |
|------|--------------|-------------------|--------|
| 10   | 1/20/45..... | 9                 | 5.10   |
|      | 1/20/45..... | 0                 | 5.12   |
| 12   | 6/13/44..... | 4                 | 2.25   |
| 16   | 6/23/44..... | 112               | 2.98   |
| 29   | 8/10/44..... | 10                | 1.62   |
| 31   | 6/26/44..... | 45                | 3.12   |
| 32   | 7/21/44..... | 48                | 1.85   |
|      | 8/10/44..... | 28                | 1.63   |
|      | 8/23/44..... | 15                | 2.87   |

TABLE 7.—*Reversibility of Level of Blood Phenol*

| Case | Date    | Diagnosis and Therapy                                       | Urea | Uremic Symptoms | Phenol |
|------|---------|---|------|-----------------|--------|
| 9    | 7/24/44 | Carcinoma of the urethra; complete retention..              | 58   | ++++            | 3.20   |
|      | 7/27/44 | 1 day postoperatively after cystostomy .....                | 37.5 | 0               | 1.85   |
| 11   | 6/14/44 | Carcinoma of the prostate; obstructive uropathy .....       | 134  | ++++            | 2.85   |
|      | 6/19/44 | Drainage by catheter; forced fluids .....                   | 76   | +++             | 2.40   |
|      | 6/28/44 | Drainage by catheter; forced fluids .....                   | 38   | 0               | 2.85   |
|      | 7/ 3/44 | 3 days postoperatively after transurethral resection .....  | 52   | 0               | 1.51   |
|      | 7/18/44 | 18 days postoperatively after transurethral resection ..... | 32   | 0               | 1.62   |
| 13   | 6/15/44 | Benign prostatic hypertrophy; complete retention .....      | 154  | +++             | 10.80  |
|      | 6/16/44 | Cystostomy; fluids administered intravenously..             | 124  | +++             | 4.85   |
|      | 6/19/44 | Fluids administered intravenously .....                     | 38   | ?               | 2.85   |
|      | 6/22/44 | Fluids administered intravenously .....                     | 24   | ?               | 3.80   |
|      | 7/ 8/44 |   | 15   | 0               | 1.60   |
| 17   | 8/ 4/44 | Benign prostatic hypertrophy; complete retention .....      | 95   | ++++            | 7.20   |
|      | 8/ 9/44 | Postoral lactate; forced fluids; drainage by catheter ..... | 18.5 | 0               | 1.90   |
|      | 8/12/44 | 2 days postoperatively after transurethral resection .....  | 29   | 0               | 1.80   |
|      | 8/18/44 |   | 46   | 0               | 1.63   |

42 mg. per hundred cubic centimeters, and that for phenol was 1.85 mg. per hundred cubic centimeters, there being pronounced (4 plus) uremic symptoms present.

The question also arises as to whether or not the level of blood phenol is of prognostic value. Table 6 shows the patients who died.

and table 7 demonstrates the reversibility of the level of phenol in the blood.

The reversibility of the level of phenol in the blood even when high levels are present, as in cases 13 and 17, indicates that the test cannot be of significant prognostic import.

Since this report embodies relatively few cases, the results are not conclusive. While we have not been able to demonstrate constancy of elevated phenols in association with uremic symptoms, we do know that there is a definite relation of increased phenol to nitrogen retention. In the light of experimental studies of other investigators, one questions whether phenol alone is responsible for the narcotic symptoms of uremia. Since guanidine has been indicted as a factor, simultaneous studies of this substance and phenol would be of value. Also, other investigators measured not only phenol but other related substances, and it is feasible that it is the total of phenol and its derivatives which actually produces the narcotic effect. Certainly, the exact role of phenol in the uremic state has not been completely ascertained, and the question is open for further investigation.

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#### CORRECTION

In the article by Dr. George A. Johnstone and Dr. John E. Ostendorph entitled "Cholecystitis with Perforation," which appeared in the July issue (*ARCH. SURG.* 53:1, 1946), the following footnote was omitted:

The unabridged version of this article was accepted to meet the thesis requirements for the degree of M.Sc. (Med.) for graduate work in surgery at the Graduate School of Medicine, University of Pennsylvania [by Dr. Ostendorph].

## SURGICAL TREATMENT OF THE PATENT DUCTUS ARTERIOSUS

Report of Five Cases

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SINCE 1907, the possibility of operation in the treatment of the patent ductus arteriosus has been recognized. Graybiel, Strieder and Boyer<sup>1</sup> made the first surgical attempt at closure of the ductus. The condition was complicated by the presence of bacterial endarteritis. The unsuccessful outcome was due to fatal hemorrhage at the operating table. Since this first attempt Gross<sup>2</sup> has ligated or divided the ductus in 133 patients with only five fatalities.

In reviewing the literature on this subject, one is impressed by the rapid advancement made in the accuracy of diagnosis and the perfection of the surgical technic. The early criteria for operation, namely, absence of infection, absence of embolic phenomena and sterile cultures of the blood no longer need be followed. The surgical treatment encompasses more and more the group of patients previously denied operation because of the presence of infection superimposed on the patent ductus.

The purpose of this paper is to add 5 cases to the literature and to discuss some problems in the preoperative and postoperative care of these patients. Each patient in this group was individual enough in the problems of therapy to warrant separate comment. The changes in therapy have more or less followed the advancement in chemotherapeutic agents and more recently the addition of biologic agents.

The literature on the subject of patent ductus arteriosus has been thoroughly summarized both from a medical and from a surgical view-

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From the Department of Surgery, Bowman Gray School of Medicine of Wake Forest College.

1. Graybiel, A.; Strieder, J. W., and Boyer, N. H.: An Attempt to Obliterate the Patent Ductus Arteriosus in a Patient with Subacute Bacterial Endarteritis. *Am. Heart J.* **15**:621, 1938.

2. Gross, R. E.: Paper read at the Meeting of the American Association for Thoracic Surgery, Detroit, May 1946.

(Footnotes continued on next page)

point by Burch<sup>3</sup> and Shapiro and Keys.<sup>4</sup> The embryology, physiology, clinical features and laboratory findings have been fully discussed in the excellent papers of Bullock, Jones and Dolley<sup>5</sup> and Gross.<sup>6</sup> This congenital anomaly when present alone or complicated by bacterial endarteritis carries a serious prognosis. The studies of Shapiro and Keys<sup>4</sup> have shown the end results in cases in which the patients were untreated. Shapiro and Keys<sup>4</sup> have found that 86 per cent of patients with this cardiac lesion died of causes directly attributable to their heart disease. They discussed a series of 140 patients operated on, with an over-all mortality rate of 8.5 per cent in cases uncomplicated by bacterial endarteritis. Thirty-three patients in their collected series had bacterial endarteritis at the time of operation. A 50 per cent rate of cure was obtained in the infected group. These figures lead one to believe that surgical intervention for this arteriovenous fistula should be attempted whenever possible.

The indications for operation are generally listed to include the following symptoms: physical retardation, cardiac failure, cardiac embarrassment without frank failure and a patent ductus plus superimposed bacterial endarteritis. It seems that this is not inclusive enough. This anomaly is certainly one instance in which prophylactic surgical treatment could be practiced, with great benefit. By now, the published articles have demonstrated the end results in untreated patients. Operation should not be denied to patients because of fear of a surgical mortality. Their chances of normal longevity if untreated are far less than their chances if operation is done. The mortality rate of 86 per cent in untreated patients as compared with 8.5 per cent in treated patients strengthens the argument. Burch<sup>3</sup> stated, "the surgical risk is still too great in average hands to recommend surgery in all patients with patent ducti." Any surgeon experienced in thoracic surgery is capable of performing this operation. Once the diagnosis of this lesion has been made operation should be the treatment of choice.

Bullock, Jones and Dolley<sup>5</sup> and Gross<sup>7</sup> have shown that the younger patients are more easily handled from a technical viewpoint and the

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3. Burch, G. E.: Congenital Patent Ductus Arteriosus: An Evaluation of its Surgical Treatment, *M. Clin. North America* **28**:388, 1944.

4. Shapiro, M. J., and Keys, A.: The Prognosis of Untreated Patent Ductus Arteriosus and the Results of Surgical Intervention: A Clinical Series of Fifty Cases and Analysis of One Hundred and Thirty-Nine Operations, *Am. J. M. Sc.* **206**:174, 1943.

5. Bullock, L. F.; Jones, J. E., and Dolley, F. S.: The Diagnosis and the Effects of Ligation of the Patent Ductus Arteriosus, *J. Pediat.* **15**:786, 1939.

6. Gross, R. E.: Surgical Closure of the Patent Ductus Arteriosus, *J. Pediat.* **17**:716, 1940.

7. Gross, R. E.: Complete Surgical Division of the Patent Ductus Arteriosus; A Report of Fourteen Successful Cases, *Surg., Gynec. & Obst.* **78**:36, 1943.

ductus easily approached and more amenable to ligation or division. Shapiro and Keys<sup>4</sup> have suggested that the probability of bacterial endarteritis increases with age. This further supports the plea for early surgical intervention.

The accuracy with which the diagnosis of the patent ductus arteriosus can be made is well illustrated by the work of Gross,<sup>7</sup> Bullock and associates<sup>5</sup> and others. Shapiro and Keys<sup>4</sup> found only two instances of mistaken diagnosis in the literature. There is no way of estimating the conditions that are wrongly diagnosed but not reported. In this series of 5 cases, the diagnosis was proved correct in all instances. Diagnosis and the preoperative preparation of these patients were entirely the work of the medical department. A great deal of credit is due them for the excellent preparation of these extremely sick patients. The results in this group of patients were dependent on their excellent physical condition prior to the operative day. In only 1 patient was there any question as to the diagnosis. Clinically the diagnosis was made by the medical staff, although the roentgenologic and laboratory studies were not confirmatory. The remaining 4 cases were clearcut in their diagnostic findings. It has been found that the history and physical examination are the most definite aids in making the diagnosis of a patent ductus arteriosus. All these patients had been told at an early age that there was something wrong with their heart. Four of the 5 patients had complications of their cardiac lesion, namely, infection, with or without emboli. Each patient presented the classic thrill over the heart, maximum to the left of the sternum in the second and third intercostal spaces, and a continuous machinery murmur with systolic accentuation in the same area. A systolic murmur at the apex of the heart was present in 4 of the 5 cases. All but 1 patient had cardiac enlargement by clinical examination. This was confirmed at the time by fluoroscopic examination. All these patients had a widened pulse pressure with a lowered diastolic pressure. Four of the 5 patients had congestion of the left lung, enlargement of the pulmonary conus and a hilar dance demonstrated by roentgenologic and fluoroscopic examination of the heart and lungs. In 3 cases septicemia was proved preoperatively with the culture of *Streptococcus viridans*. In 1 case bacterial endarteritis was not present. In 1 case the clinical picture of septicemia was present, with multiple pulmonary infarcts and a splenic infarct, but no organisms were grown on culture of the blood.

All 5 patients were admitted to the medical service of the North Carolina Baptist Hospital and transferred to the surgical service at the time of the operation. The youngest patient was 18 years old, and the oldest patient was 30 years. The youngest patient did not have bacterial endarteritis. It is interesting to note that with the exception of the youngest patient each patient had not only bacterial endarteritis but also

embolic accidents previous to operation. In the following paragraphs the cases are presented in chronologic order on the basis of the date of operation.

CASE 1.—The patient was a 28 year old factory worker who had had "heart trouble" all his life. Prior to the present illness the patient had always been well. It had never been necessary for him to restrict his activities. There was no history of dyspnea on exertion or orthopnea. The patient had never noticed cyanosis.

On physical examination the patient had a temperature of 102 F. His pulse rate was 110 and his blood pressure 140 systolic and 56 diastolic. Scattered petechiae were seen over the skin and mucous membranes and beneath the nail beds. The heart was enlarged to the left, and on auscultation the classic murmur and thrill of a patent ductus arteriosus were heard and felt.

Laboratory studies revealed mild secondary anemia, with a leukocytosis of 16,000. A roentgenogram of the chest showed some hilar consolidation of the left lung. The pulmonary conus was prominent, and on fluoroscopic examination a hilar dance was demonstrated. An electrocardiogram was reported as normal. Cultures of the blood the day of admission produced fifty colonies of *Str. viridans* per cubic centimeter. On four successive days repeated blood cultures of the blood showed the same results. On the second hospital day the patient experienced sudden, sharp pain in the right side of the chest.

On physical examination at this time a pulmonary infarct in the periphery of the lower lobe of the right lung was found. This was substantiated by the roentgenologic findings. He was given large doses of sulfanilamide by mouth; his blood sulfanilamide level was maintained at approximately 12 mg. per hundred grams. There was a definite reduction in the number of colonies of *Str. viridans*, but cultures of the blood never became sterile.

He was operated on, and a patent ductus arteriosus was found and doubly ligated with braided silk. His postoperative course was not remarkable. Cultures of the blood remained sterile from the day of operation. The patient was discharged on his fourteenth postoperative day, with a well healed wound and symptom free.

*Comment.*—This patient was operated on in the prepenicillin era. Use of the chemotherapeutic agents at hand was unsuccessful in sterilizing the blood stream. Accordingly, he was operated on in the presence of fever and bacterial endarteritis. At the time of operation the patient was malnourished, had a definite loss of weight and in general was a poor surgical risk. He is alive and well three years after operation. There is no cardiac murmur or thrill at the present time.

CASE 2.—The patient was a 25 year old mill worker, admitted because of fever, generalized malaise, weakness and loss of weight over a period of six months. A diagnosis of subacute bacterial endocarditis was made before entry.

The past history was noncontributory. He had been told as a young boy that he had a "leaking heart."

On physical examination the temperature was 103 F., pulse rate 120, respiratory rate 20 and the blood pressure 120 systolic and 40 diastolic. He presented the classic findings of a patent ductus arteriosus. There was evidence of cardiac enlargement on the right and left sides. The pulse was Corrigan in type. There were scattered petechiae over the mucous membranes. Neurologic examination suggested a cerebral embolus involving the arm and forearm centers in the right cerebral cortex.

The laboratory findings showed no anemia or leukocytosis. The sedimentation rate was 53 mm. per hour corrected. Cultures of the blood produced twenty to twenty-five colonies of *Str. viridans* per cubic centimeter. The electrocardiogram showed ventricular hypertrophy on the left side. The roentgenogram of the chest showed cardiac enlargement and hilar pulmonary congestion on the left side.

Sulfadiazine was given orally in doses of 6 Gm. every twenty-four hours. After several days the temperature and pulse were normal, although the cultures of the blood remained positive. Operation was advised, but the patient decided against this and left the hospital. He was readmitted six weeks later, with a return of all his symptoms. His temperature was 102 F. At this time the hemoglobin content was 60 per cent, with 3,300,000 red blood cells. Cultures of the blood remained positive for *Str. viridans*. He was given two small transfusions of blood to prepare him for operation. In vitro studies of the organisms in the blood showed no sensitivity to sulfadiazine, sulfathiazole or sulfapyridine, and accordingly no chemotherapy was given. The day of operation cultures of the blood produced forty-five colonies of *Str. viridans* per cubic centimeter. The patient had a patent ductus at operation, which was ligated doubly with heavy, braided, black silk.

This patient was admittedly a poor operative risk. He had already suffered a cerebral embolus and had had a prolonged febrile course prior to operation. The postoperative course was stormy. Although the blood stream became sterile after ligation of the patent ductus the patient progressed steadily downhill, and he died on the fourth postoperative day. Forty-eight hours postoperatively *Str. viridans* was again cultured from the blood stream. At autopsy numerous infarcts were found in the spleen, small bowel and cerebrum. Vegetations were present on the aortic valves, from which *Str. viridans* organisms were cultured. The patent ductus was firmly occluded, and the ligatures were intact.

*Comment.*—The presence of cerebral emboli, preoperatively, the long-standing septicemia and the positive cultures of the blood following operation all contributed to his death. Operation was done because it was believed to offer the only chance this patient had for survival. The findings at autopsy, of course, explain the reasons for the persistently positive cultures of the blood. If penicillin had been available at the time of operation, perhaps this focus on the aortic valves could have been controlled.

CASE 3.—A 24 year old housewife was admitted because of weakness, malaise, loss of weight, elevated afternoon temperature and "rheumatism," of three months' duration. There had been a known cardiac lesion present since the age of 3 months. Previous to admission to the North Carolina Baptist Hospital, the patient had been treated with penicillin. A diagnosis of congenital cardiac lesion with superimposed bacterial endocarditis had been made. There had been no improvement in the general condition of the patient.

Five weeks prior to admission there developed pain in the left side of the chest, rusty sputum and spiking fever. A diagnosis of pulmonary infarction was made. The patient during this time noticed petechiae under her nail beds. The administration of penicillin was continued, without improvement, until her admission to the North Carolina Baptist Hospital.

On physical examination a temperature of 101 F., pulse rate of 104 and respiratory rate of 22 were found. The blood pressure was 94 systolic and 56 diastolic. The weight was 75 pounds (34 Kg.). Scattered petechiae were found in the buccal mucous membranes and in the nail beds. The lungs were clear, and no friction



rub was heard. The heart was enlarged to percussion. To the left of the sternum, in the second intercostal space, the classic murmur and thrill of a patent ductus arteriosus were found. The abdomen was normal except for the presence of a scar low in the midline. There was no clubbing of the extremities.

Accessory laboratory findings were a hemoglobin content of 10 Gm., with 3,100,000 red blood cells, and a white blood cell count of 17,000, with 17 per cent young polymorphonuclear leukocytes. The sedimentation rate was 47 mm. per hour corrected. Cultures of the blood produced fifty colonies of *Str. viridans* per cubic centimeter. Fluoroscopic examination of the chest showed the cardiac pulsations to be excessively active. There was some fulness in the region of the pulmonary conus. The sign of a hilar dance was present.

Penicillin in concentrations of 1 Oxford unit per cubic centimeter completely inhibited growth of the organisms cultured from the blood stream. With knowledge that previous penicillin therapy had been ineffectual in sterilizing the blood stream, this patient was given continuous intramuscular penicillin drips, receiving 240,000 Oxford units every twenty-four hours. Improvement was rapid. Within seventy-two hours, the temperature curve was normal and cultures of the blood were sterile. Several small transfusions were given and the patient transferred to the surgery.

At operation, a patent ductus measuring 10 mm. in length and 7 mm. in width was found. It did not prove to be abnormally friable. Visceroparietal adhesions were numerous but fine and easily freed. The ductus was divided between clamps and the ends oversewn. The chest was closed without drainage. Postoperatively the patient was afebrile after twenty-four hours, and the left lung was completely reexpanded by roentgenologic study. The patient was allowed to go home on the twelfth day. Daily cultures of the blood taken postoperatively were sterile. Penicillin was continued for twenty-four hours after operation. Six months later the patient was entirely well and had gained 25 pounds (11.3 Kg.).

*Comment.*—This was the first patient operated on after penicillin became available for civilian use. It was also the first time that the ductus was severed completely by us. This patient was certainly a better operative risk, probably as a result of penicillin therapy. She was operated on when free of symptoms and afebrile and in the presence of a good nutritional state. The case also illustrates the value of *in vitro* studies in the use of biologic agents and the ever present variable factor of blood concentrations during penicillin therapy.

CASE 4.—An 18 year old married girl had been told at the age of 12 years that she had heart trouble. One year prior to admission she was refused life insurance because of heart disease. She was constantly aware of a humming in her chest, which was greatly accentuated by activity.

Results of physical examination were entirely normal except for abnormal cardiac findings. There was a continuous machinery-like murmur in the second and third left intercostal spaces, with a systolic accentuation. There was a palpable thrill over the same area.

Accessory clinical findings showed no anemia or leukocytosis. Fluoroscopic and roentgenologic examination of the chest showed some enlargement of the heart, principally of the left ventricle. There was no enlargement of the pulmonary conus, and no hilar dance was seen.

The indication for operation of this patient was, first, the presumed presence of a patent ductus arteriosus and, second, the findings of early cardiac enlargement. At operation the ductus was found to be short and wide. It measured

less than 2 mm. in length and approximately 4 mm. in width. It was impossible to divide because of its short length. Efforts to increase its length by subadventitial dissection, as proposed by Touroff,<sup>8</sup> were not successful. In addition the patient presented a saccular aneurysm of the pulmonary artery proximal to the patent ductus. Four plicating sutures of no. 00000 waxed arterial silk were used to occlude the lumen. This obliterated the murmur.

This case represented the only instance of the posterolateral approach to the ductus, as recommended by Harrington.<sup>9</sup> The reason for using this approach was that this girl had large pendulous breasts and incision above or below the mammary gland would have required extensive dissection.

The patient's chest was closed without drainage. Her postoperative course was uneventful. She was discharged from the hospital on her ninth postoperative day. At present, six months later, she is symptom free. On examination, however, there was a distant soft murmur at the second left interspace. Whether this represents a recurrence or a murmur associated with the pulmonary aneurysm found at operation is not known. Such murmurs have been heard at the operating table after the ductus has been completely severed and are presumably due to a swirling of blood in the stump of the ductus on the pulmonary end.

*Comment.*—This case illustrates the variable pathologic conditions found in any group of congenital cardiac lesions. It will take time to tell whether or not this patient was benefitted by operation.

CASE 5.—A 30 year old housewife was admitted with complaints of diarrhea, fever and chills of seven weeks' duration. There had also been considerable cough, blood-streaked sputum and thoracic pain. Her health prior to this time had been good.

Her past history was that she had been treated for "ulcer of the stomach" for five years. She had never been incapacitated by this lesion and carried on her work without difficulty.

On physical examination the temperature was 103 F., pulse rate 120 and respiratory rate 20. The blood pressure was 120 systolic and 70 diastolic. She presented the typical thrill and murmur of a patent ductus arteriosus. There were changes in the left pulmonary field and pleura compatible with pulmonary infarction. Examination of the abdomen was noncontributory. There was no clubbing or cyanosis of the extremities.

The accessory laboratory findings were not remarkable. Roentgenograms of the chest showed areas of fibrosis in the periphery of both pulmonary fields, which were interpreted as being healed pulmonary infarcts. The pulmonary conus was enlarged, and the hilar dance was present. A series of roentgenograms of the gastrointestinal tract showed a healing duodenal ulcer, without obstruction. Repeated cultures of the blood were sterile. Agglutinations for typhoid and paratyphoid fever gave negative results.

In spite of sterile cultures of the blood it was felt that this patient had bacterial endarteritis superimposed on a patent ductus arteriosus. She was given penicillin, 20,000 Oxford units intramuscularly every three hours. This was increased to

8. Touroff, A. S. W.: The Results of Surgical Treatment of Patency of the Ductus Arteriosus Complicated by Subacute Bacterial Endarteritis, *Am. Heart J.* 25:187, 1943.

9. Harrington, S. W.: Patent Ductus Arteriosus with Bacterial Endarteritis: Transpleural Ligation Through Posterolateral Approach: Report of a Case, *Proc. Staff Meet., Mayo Clin.* 18:217, 1943.

60,000 units every three hours when she failed to improve clinically on the smaller dose. Her temperature returned to normal, and there was striking subjective improvement. During her stay in the hospital she was given aluminum hydroxide gel and tincture of belladonna to control her ulcer, along with a special diet. She asked release from the hospital at Christmas and returned to the hospital after the holiday for operation. At home a daily temperature chart showed no elevation of temperature.

She was readmitted for operation. The patent ductus was the largest in this series, measuring 15 mm. in length and 11 mm. in width. It was easily divided between clamps and the ends oversewn with fine, black, waxed silk.

Her postoperative course was uneventful. She was discharged afebrile and generally improved on her tenth postoperative day. The murmur has not recurred, nor has she had recurrence of fever. She is well six months after operation. The causative organisms were never proved in this case.

*Comment.*—This case was puzzling from a bacteriologic standpoint, because it was never possible to demonstrate organisms in the blood stream in spite of a clinical picture of septicemia. Her response to penicillin was certainly suggestive of septicemia and the postoperative result seemed conclusive.

#### COMMENT

The use of penicillin in the treatment of bacterial endarteritis is not new. The more recent medical literature contains reports of successful treatment of this disease with penicillin. To date there has been nothing reported in the surgical literature about the use of penicillin in the treatment of the patent ductus with superimposed bacterial endarteritis prior to the surgical intervention of this fistula. The course of patients treated with penicillin has been impressive compared with that of those operated on with positive cultures of the blood and no penicillin. Certainly a large series will most likely show more failures, but when in vitro studies show organisms in the blood stream sensitive to penicillin its use should constitute the primary goal of preoperative preparation.

Touroff<sup>10</sup> in 1942 advised early ligation in the cases of patent ductus with infection. He stated that chemotherapy is of no help in controlling the disease process. This viewpoint must be altered with the advent of penicillin. One case in this group illustrates the variability of penicillin therapy. How much penicillin and how long it is to be given must be determined by the clinical course of the patient.

The patients in the first 2 cases perhaps have been greatly benefited by preoperative sterilization of the blood stream. A patient with loss of weight, fever and septicemia presents alone a formidable surgical risk. Certainly it is desirable to have these patients in the best of physical condition before surgical treatment of the patent ductus is attempted. Gross<sup>7</sup> suggested that patients who were proved to have embolic acci-

10. Touroff, A. S. W.: Further Experiences in the Surgical Treatment of Subacute Streptococcus Viridans Endarteritis Superimposed on Patent Ductus Arteriosus, *J. Thoracic Surg.* 12:1, 1942.

dents were poor surgical risks and should not be subjected to operation. Touroff<sup>8</sup> stated the belief that this does not contraindicate operation. He reported 4 cases in 1943 with successful recovery following surgical ligation of the patent ductus. All his patients had embolic accidents prior to operation. This report adds 3 cases to this group. The use of penicillin will help reduce the mortality rate, and thus operation can be offered to that group of patients denied surgical treatment because of the risk. This small group of patients suggests that there is some advantage to penicillin therapy. More operations must be done before any definite conclusions can be made.

The operative procedures have been standardized by Gross.<sup>7</sup> The procedure in this group is essentially the same. Four of the 5 patients were operated on through an anterior incision, with subperiosteal resection of the anterior two thirds of the costal cartilage and rib. One patient was operated on through the posterolateral approach, as recommended by Harrington.<sup>9</sup> There were 2 men and 3 women in this series. The opinion that incision above the breast will destroy a major portion of the blood supply and lead to atrophy of the breast may not be well founded. Numerous pneumonectomies have been performed through a similar anterior incision without much difficulty; however, most of these patients were in the older age group. There has been no instance of atrophy of the female or male breast from such an incision. Review of the anatomy of this region reveals adequate circulation laterally and from below to supply the mammary tissue. None of these patients complained of numbness in the breast. Nixon<sup>11</sup> recommended intercostal incision without rib resection for exposure of the patent ductus. We have not used the intercostal incision.

The ductus was doubly ligated in the first 2 cases, severed between clamps and the ends oversewn in 2 cases and plicated in 1 case. It is obvious that division of the patent ductus should be the procedure of choice when possible. Ligation in continuity is simpler and certainly safer but does not absolutely rule out the possibility of recurrence. A satisfactory clamp which is dependable has not been advised. At present such a clamp is being made, which it is hoped will be satisfactory. The patent ductus is so variable in size that no uniform method of division or ligation can be anticipated. Of the 5 cases 1 could have been ligated as suggested by Blalock.<sup>12</sup> Cellegane or sclerosing agents injected between ligatures has not been used in any of these patients.

11. Nixon, J. N.: Surgical Closure of the Patent Ductus Arteriosus, *Texas State J. Med.* 40:473, 1945.

12. Blalock, A.: Operative Closure of the Patent Arteriosus, *Surg., Gynec. & Obst.* 82:113, 1946.

In the group of patients with bacterial endarteritis the ductus varied in length and width, but in none was it excessively friable. It should be noted that the 2 cases in which the ductus was divided between clamps represented cases complicated by bacterial endarteritis.

The mediastinal pleura was closed in the last 3 cases, since it was felt that the area was sterile due to the penicillin therapy. Mediastinitis was thus not feared. The chest was closed without drainage. The air in the pleural space was removed by catheter suction through a catheter left in the pleural space during closure. This was removed after the thoracic incision was completely closed. Although 4 of the 5 patients had previous pulmonary infarcts, visceroparietal pleural adhesions were never a great problem.

#### SUMMARY

Five patients were operated on with ligation or division of the patent ductus arteriosus. There was one death in this group. Four of the 5 patients had subacute bacterial endarteritis complicating their congenital cardiac disease. These same 4 patients had preoperative embolic accidents, the chief site being the lung. Penicillin was satisfactorily used in controlling the septicemia in the last few patients.

#### CONCLUSIONS

Penicillin has materially aided in reducing the mortality rate of patients with subacute bacterial endocarditis superimposed on a congenital patent ductus arteriosus.

The severance of the patent ductus is preferable to ligation in continuity when possible.

The anterior approach to the mediastinum, with rib resection, has proved satisfactory.

The patent ductus arteriosus should be corrected more frequently when found.

Embolic accidents do not usually contraindicate operation for the patent ductus arteriosus.

# LYMPHOGRANULOMATOUS STRICTURES OF THE RECTUM

A Résumé of Four Hundred and Seventy-Six Cases

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**L**YMPHOGRANULOMA venereum and particularly strictures of the rectum caused by this disease have been the subject of many reports in recent years. It is generally recognized that the anorectal manifestations of this widespread disease offer the most serious threat to life and are, likewise, most difficult to treat satisfactorily. At Harlem Hospital we have had an opportunity to study a large number of cases of fibrous inflammatory strictures of the rectum, and this paper is a study of 476 consecutive cases in which patients were admitted to the wards of the hospital during the fifteen and a half year period from Jan. 1, 1930, to Aug. 1, 1945. The more attention we have given this disease, the more we have come to realize that our knowledge is still extremely incomplete and that increased clinical and laboratory study is needed to clear up many aspects of the subject. Some clinical aspects of this disease have been treated by members of the staff of this hospital in previous papers.<sup>1</sup>

## HISTORICAL SUMMARY

Brief mention should be made of the early history of this important and increasingly interesting disease and its rectal manifestations.

As early as 1824 Martland,<sup>2</sup> a Scottish surgeon, performed an iliac colostomy on the left side, for obstruction due to a stricture, and his patient lived for seventeen years.

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From the Surgical Service of Harlem Hospital, Dr. Louis T. Wright, Director.

1. (a) Kassebohm, F. A., and Schreiber, M. J.: Spontaneous Delivery Complicated by Rectal Stricture, Rectovaginal Fistula and Rupture of the Rectum, *Am. J. Obst. & Gynec.* **31**:674 (April) 1936; (b) Management of Labor Complicated by Rectal Stricture, *New York State J. Med.* **37**:484 (March 1) 1937. (c) Wright, L. T., and Logan, M.: Osseous Changes Associated with Lymphogranuloma Venereum, *Arch. Surg.* **39**:108 (July) 1939. (d) Levy, J. G.; Holder, E. C., and Bullock, J. G. M.: Stricture of the Rectum Due to Lymphogranuloma Venereum: Symptoms and Treatment with Sodium Sulfanilyl Sulfanilate, *Am. J. Digest. Dis.* **9**:237 (July) 1942. (e) Wright, L. T.; Berg, B. N.; Bolden, J. V., and Freeman, W. A.: Rectal Strictures Due to Lymphogranuloma Venereum

(Footnotes continued on next page)

Hugier,<sup>3</sup> in 1848, was the first to describe an eroding phagedenic elephantiasis of the vulva, often accompanied with ulceration of the perineum, anus and lower part of the rectum, which he thought was due to tuberculosis, and he named it "esthiomene."

One year later, in 1849, Larsen,<sup>4</sup> a Danish surgeon, described rectal stricture in 11 women.

The first external rectotomy operation for rectal stricture was performed by Humphry<sup>5</sup> in 1856, and he stated that results in 2 of his cases were successful. This operation was reintroduced to the medical profession in 1872 by Verneuil.<sup>6</sup>

Gläser<sup>7</sup> reported the first excision operation for stricture of the rectum, in 1864. In 1867 Gläser performed a lumbar colostomy of the left side on this same patient because of intestinal obstruction due to the stricture which he had already excised and which had recurred. Twenty years later, in 1887, he did an autopsy on the same patient and found that the pelvic colon and rectum had been reduced to nothing more than a long, narrow fibrous cord perforated by a small canal, which would admit only the smallest sounds and was surrounded by inflammatory tissue.

Curling<sup>8</sup> was the first American surgeon to perform a lumbar colostomy for obstruction due to an incurable stricture, in 1865.

In 1875, Fournier,<sup>9</sup> the famous French syphilologist, described strictures of the rectum, with great accuracy, and stated that they were caused by syphilis; this was due to the fact that most of the patients

with Especial Reference to Pauchet's Excision Operation, Surg., Gynec. & Obst. 82:449 (April) 1946.

2. Martland, R.: A Case, Edinburgh M. & S. J. 24:271, 1825; cited by Tuttle.<sup>11</sup>

3. Hugier, P. C.: Memoire sur l'esthiomene ou dartre rongeante de la vulvoanale, Mém. Acad. de méd. 14:501, 1848; cited by Nelson, N. A., in Virus, and Rickettsial Diseases, Cambridge, Mass., Harvard University Press, 1940, p. 365.

4. Larsen, S. J.: Praktiske bemaerkinger over stricture i masttarmen, Hosp.-Medd. 2:289, 1849; cited by Jersild, O.: Notice historique sur l'infiltration hyperplasique du rectum avec rétrécissement fibreux et sur l'origine prétendue syphilitique de cette affection, Ann. de dermat. et syph. 7:74 (Feb.) 1926.

5. Humphry, G. M.: Three Cases of Stricture of the Rectum, Treated by Incision, Assoc. M. J., London, 1856, p. 21; cited by Hartmann.<sup>10</sup>

6. Verneuil: Rétrécissements du rectum; traitement par la rectotomie verticale, Bull. Soc. de chir. de Paris 1:447, 1872; cited by Hartmann.<sup>10</sup>

7. Gläser, J. A.: Stricture des Mastdarmes mit Mastdarm-Scheidenfistel, Arch. f. klin. Chir. 9:509, 1868; 34:459, 1887; cited by Hartmann<sup>10</sup> and by Tuttle.<sup>11</sup>

8. Curling, T. B.: Correspondence, Am. J. M. Sc. 91:575, 1873; cited by Tuttle.<sup>11</sup>

9. Fournier, A.: Lésions tertiaires de l'anus et du rectum, Paris, A. Delahay, 1875.

who showed the disease also had coexistent syphilis, and he termed the condition "anorectal syphiloma."

Henri Hartmann,<sup>10</sup> of Paris, was the first surgeon to comprehend the disease fully. He performed sixteen external rectotomy operations, with unsuccessful results, early in his career, and in 1895 he reported thirty-five excision operations with successful results. In 1930 he made a report of sixty-six excision operations for rectal stricture. He wrote many articles on the subject and reported numerous clinical histories of cases, which represent the best clinical study of rectal strictures that has been published, and this in spite of the fact that he knew nothing about the Frei test, the true etiologic agent or the systemic nature of the disease. Hartmann had careful histopathologic studies made of all specimens removed at operation, and the pathologic work of M. Toupet was exceptionally detailed and thorough.

Tuttle,<sup>11</sup> in this country, in 1902, described rectal strictures, with great accuracy, although he, like Fournier and Hartmann, did not know their true cause and therefore employed the generic term "inflammatory strictures." Tuttle did not enter into the field of active controversy as to whether these strictures were due to gonorrhea, syphilis or tuberculosis, but he did state unequivocally that all these strictures were preceded by ulceration.

Two contributions stimulated great interest in this disease, namely, the description by Durand, Nicolas and Favre,<sup>12</sup> of Lyons, in 1913, of the disease as a distinct clinical entity and the introduction by Wilhelm Frei<sup>13</sup> of his intracutaneous test. This interest has continued up to the present time.

Frei and Koppel,<sup>14</sup> in 1926, brought forward evidence that proved that the occurrence of benign strictures of the rectum and elephantiasis of the genitals was of lymphogranulomatous origin, by means of Frei's intradermal test. Their work was confirmed by Bensaude and

10. Hartmann, H.: *Chirurgie du rectum*, Paris, Masson & Cie, 1931, p. 166; *L'extirpation des rétrécissements inflammatoires du rectum*, Bull. et mém. Soc. nat. de chir. **56**:855 (June 28) 1930.

11. Tuttle, J. P.: *Diseases of Anus, Rectum and Pelvic Colon*, New York, D. Appleton and Company, 1903, p. 463.

12. Durand; Nicolas, J., and Favre: *Lymphogranulomatose inguinale subaigue*, Bull. et mém. Soc. méd. d. hôp. de Paris **35**:274 (Jan. 31) 1913.

13. Frei, W.: *Eine neue Hautreaktion bei Lymphogranuloma inguinale*, Klin. Wchnschr. **4**:2148 (Nov. 5) 1925; *Die Elephantiasis genito-anorectalis (Esthiomène und entzündliche Rektumstriktur)*; *Eine Teilkrankheit der Lymphogranulomatosis inguinalis*, *Ergebn. d. ges. Med.* **21**:113, 1936; *Venereal Lymphogranuloma*, J. A. M. A. **110**:1653 (May 14) 1938.

14. Frei, W., and Koppel, A.: *Ulcus vulvae chronicum elephantasticum (Esthiomene) und sogenanntes Syphilome anorectal als Folgeerscheinungen der Lymphogranulomatosis inguinalis*, Klin. Wchnschr. **7**:2331 (Dec. 2) 1928.



Lambling.<sup>15</sup> Hellerstrom and Wassen,<sup>16</sup> in 1930, by means of intracerebral inoculation of monkeys, proved that the disease was due to a filtrable virus. Their work has been amply proved by innumerable workers throughout the world. Today the virus is demonstrable microscopically and can be grown on chick embryo mediums.

The disease has also been found to be worldwide in its distribution.

Although the early manifestations of this disease are not within the scope of this paper, it has been shown that the genitalia, anorectal region, eyes, mouth, pharynx, larynx, cervical glands, female urethra, male urethra, colon, ileum, ovaries, fallopian tubes, meninges, intra-abdominal glands, joints and bones may be involved.

TABLE 1.—Incidence of Rectal Strictures as Regards Race and Sex

| Author  | Cases,<br>No. | White |      | Negro    |      | Men                       |      | Women    |      |
|---|---------------|-------|------|----------|------|---------------------------|------|----------|------|
|   |               | No.   | %    | No.      | %    | No.                       | %    | No.      | %    |
| Alley, R. C.: Tr. Am. Proct. Soc. 35: 150, 1934 .....   | 20            | 2     | 10   | 18       | 90   | 3                         | 15   | 17       | 85   |
| Mathewson, O., Jr.: J. A. M. A. 110: 709, 1938 .....  | 78            | 66    | 84.6 | 12       | 15.4 | 60                        | 76.9 | 18       | 23.1 |
| Grace, A. W.: J. A. M. A. 122: 74, 1943 (strictures with proctitis).....                          | 90            | ..    | .... | ..       | .... | 35                        | 36.7 | 57       | 63.3 |
| Torpin, R.; Greenblatt, R. B.; Pund, E. R., and Sanderson, E. S.: Am. J. Surg. 43: 688, 1939..... | 96            | 4     | 4.2  | 92       | 95.8 | 0                         |      | 96       | 100  |
| Splesman, M. G.; Levy, R. O., and Brotman, D. M.: Am. J. Digest. & Nutrition 3: 931, 1937.....    | 115           | 11    | 10   | 104      | 90   | 12                        | 10   | 103      | 90   |
| Bensaude and Lambling <sup>15</sup> .....   | 158           | ..    | .... | ..       | .... | 70                        | 44.3 | 88       | 55.7 |
| Hayes, H. T.: Am. J. Surg. 16: 323, 1932 .....  | 160           | ..    | 19   | ..       | 80   | ..                        | 15.8 | ..       | 84.2 |
| Woods, F. M., and Hanlon, C. R.: Ann. Surg. 120: 598, 1944.....                                   | 192           | ..    | 15   | ..       | 85   | (Ratio: 7 women to 1 man) |      |          |      |
| David, V. O., and Loring, M.: J. A. M. A.: 106: 1875, 1936.....                                   | 200           | ..    | .... | Majority |      | ..                        | .... | Majority |      |
| Martin, C. F.: J. A. M. A. 101: 1550, 1933 .....  | 227           | ..    | 18.4 | ..       | 81.6 | 0                         |      | 227      | 100  |
| Wright, Freeman and Bolden.....   | 476           | 23    | 4.8  | 453      | 95.2 | 42                        | 8.8  | 437      | 91.2 |

In table 1 is listed the incidence of rectal strictures as regards race and sex by authors who have reported large series of cases.

It is seen that in this country strictures occur largely in women, particularly Negro women, and, in men, in white pederasts. Mathewson, San Francisco, reported a predominance of the disease in white persons, but his report is the one exception. The predominant frequency of rectal stenosis in women as contrasted with that in men is due to the

15. Bensaude, R., and Lambling, A., in Discussion on the Etiology and Treatment of Fibrous Stricture of the Rectum (Including Lymphogranuloma Inguinale), Proc. Roy. Soc. Med. 29: 1441 (Sept.) 1936.

16. Hellerstrom, S., and Wassen, E.: Etude du virus de la lymphogranulomatose inguinale (maladie de Nicolas-Favre), Compt. rend. Soc. de biol. 106: 802, 1931.

difference in the lymphatic drainage. Most authors agree that stricture of the rectum in men occurs only as a result of sodomy. David and Loring are of the opinion that infection occurs in women from vaginal secretion and in men by perverted habits. Frei was of the opinion that in women sodomy was the chief cause, but with this opinion we do not agree. It is true that these conditions occur to a large extent in prostitutes and women of the lowest social strata, and is likewise a fact that many of these patients have coexisting venereal diseases, but not always. Because of the low socioeconomic status of these patients, they are to be found mainly in city hospitals. It is possible that because they belong to the lowest income group it was not until a few years ago that they began to receive intelligent and intensive scientific study, but we do know that the disease is commonest among extremely poor and illiterate persons who do not practice adequate personal hygiene and among those to whom venereal prophylaxis is unknown.

TABLE 2.—*Age Incidence*

| Age, Yr.   | Cases, No. |
|------------|------------|
| 20-30..... | 165        |
| 30-40..... | 212        |
| 40-50..... | 65         |
| 50-60..... | 28         |
| 60-70..... | 4          |
| 70-80..... | 1          |
| 80-90..... | 1          |
| Total..... | 476        |

Rosser<sup>17</sup> explained the frequency of rectal stricture in Negro women as being due to a fibroblastic diathesis of pigmented peoples and their greater tendency toward formation of scar tissue. Rosser's theory does not stand up, because of the great frequency of rectal strictures in white men who practice passive pederasty. It is a common fact that any irritating stimulus will produce a greater reaction of the fibrous tissue, such as keloids, in Negro people generally, but, nevertheless, to advance such a theory is an oversimplification of a complex problem.

In table 2 is listed the age incidence in this series of cases.

The youngest patient was 20 years and the oldest 83. It is to be noted from table 2 that the largest number of patients showing strictures of the rectum is between 30 and 40 years of age and the next largest number is between the ages of 20 and 30. This is due to the chronicity of the disease, because strictures requiring hospitalization as a rule do not develop until some years after the primary infection has

17. Rosser, C.: Proctologic Peculiarities of the Negro—The Fibroblastic Diathesis, *Am. J. Surg.* **37**:265 (Nov.) 1932; Benign Stricture of the Rectum, *Texas State J. Med.* **27**:777 (March) 1932.

occurred. Death from other concomitant diseases lessens its frequency in the later decades of life.

#### ETIOLOGY

The causative agent of the disease is a filtrable virus, which can be cultivated on chick embryo mediums. In their early work, Ravaut, Levaditi, Lambling and Cachera<sup>18</sup> inoculated monkeys with material from a patient with proliferous proctitis, and in the monkeys a typical encephalitis developed; in a second case, Laederich, Levaditi, Mamou and Beauchesne<sup>19</sup> produced a typical encephalitis in an ape which was inoculated with an emulsion from an adenopathic ganglion which had been produced in a guinea pig by implantation of a fragment of rectal mucosa from the patient.

Rodanische,<sup>20</sup> by experiments with cross immunization, indicated that there were seven strains of the virus, and, subsequently, Palmer, Kirsner and Rodaniche<sup>21</sup> identified five strains of the virus from material studied by them. These observers demonstrated the presence of the virus in rectal strictures in the rectal mucosa by biopsy in 4 cases; 1 patient had had a stricture for six years, 1 for eight, 1 for thirteen and 1 for twenty-one years, as judged by the onset of symptoms.

Coutts<sup>22</sup> stated that the virus is primarily an inhabitant of the mouth, and he attributed the growth of the disease to a growth in sexual perversion. Coutts, Martini and Landa<sup>23</sup> have postulated the existence of two viruses, which may be termed A and B. Virus A, they were of the opinion, produces inguinal adenitis, esthiomene vulvae, elephantiasis of the penis and scrotum and rectal stricture. Virus B is blamed for the constitutional symptoms, generalized lymphadenopathy, cutaneous changes and arthritis.

18. Ravaut, P.; Levaditi, C.; Lambling, A., and Cachera, R.: La présence du virus de la maladie de Nicolas-Favre dans les lésions d'un malade atteint d'ano-rectite ulcéro-végétante, *Bull. Acad. de méd., Paris* **107**:98 (Jan. 19) 1932; cited by Stannus, H. S.: *A Sixth Venereal Disease*, Baltimore, William Wood & Company, 1933.

19. Laederich, L.; Levaditi, C.; Mamou, H., and Beauchesne, H.: Rétrécissement inflammatoire du rectum, forme aberrante de la maladie de Nicolas-Favre, *Bull. et mém. Soc. méd. d. hôp. de Paris* **48**:1072 (July 4) 1932.

20. Rodaniche, E. C., cited by Palmer, Kirsner and Rodaniche.<sup>21</sup>

21. Palmer, W. L.; Kirsner, J. B., and Rodaniche, E. C.: Lymphogranuloma Venereum Infection of the Rectum, *J. A. M. A.* **118**:517 (Feb. 14) 1942.

22. Coutts, W. E.: Glossitis marginata in ihrer Beziehung zur Lymphogranulomatosis inguinalis, *Dermat. Wchnschr.* **97**:1664 (Nov. 25) 1933; cited by David, V. C., and Loring, M.: Extragenital Lesions of Lymphogranuloma Inguinale, *J. A. M. A.* **106**:1875 (May 30) 1936.

23. Coutts, W. E.; Martini, J., and Landa, F.: Lymphogranulomatosis Venerea, *Am. J. Surg.* **22**:96 (Oct.) 1933.

## PATHOGENESIS

Primary infection, as noted by Frei, David and Loring and Grace, may in men take place directly in the rectum by pederasty, and in women the primary infection takes place in the vagina or cervix, the lymphatic vessels of which drain directly into the perirectal or pelvic glands.

The so-called Jersild syndrome, which is elephantiasis genitoano-rectale, is named after Jersild,<sup>24</sup> who regarded rectal lesions as secondary to adenopathy of Gerota's ganglion and who stated that this results in perirectal lymphostasis.

Intensive study of the lymphatic drainage in the genital and anal regions has helped to clarify our knowledge as to how rectal strictures and associated lesions develop.

Gerota,<sup>25</sup> while working in Waldeyer's laboratory in Berlin, Germany, found that the anogenitoinguinal lymphatic system communicates with the rectum by multiple anastomoses and that in the lateral wall of the rectum, in all the tunica muscularis between the latter and the fascia rectipropria, immediately above the insertion of the levator ani, there are six to eight lymph glands, which receive the lymph from the lower portion of the rectum. These glands are now called the anorectal glands of Gerota.

Nesselrod<sup>26</sup> demonstrated that in women the lymphatic drainage from the external genitalia is inguinal, as in men, but that the drainage from the vagina and cervix is pelvic.

Barthels and Biberstein,<sup>27</sup> in a discussion of the genital lymphatic system, have produced data to show that the superficial lymphatic network of the vulva goes to the superficial inguinal glands and that the abundant network of the clitoris passes to the deep inguinal nodes and a few of these directly to the external iliac and hypogastric nodes. The posterior part of the vulva has, in addition, direct lymph pathways to the anal network of glands, which drain partly into the inguinal glands, partly into the anorectal glands and partly, omitting these glands, directly to the sacral lymph nodes. The lymph vessels of the lower third of the vagina, like those of the middle and upper portions, pass

24. Jersild, O.: Les intradermo-réactions dans le chancre mou et dans la lymphogranulomatoase inguinale considérées spécialement dans leurs rapports avec l'étiologie du syphilome ano-rectal, *Ann. de dermat. et syph.* **1**:577 (June 30) 1930; *Considérations sur l'intra-épidermo-inoculation de M. Ravaut*, *Bull. Soc. franç. de dermat. et syph. (Réunion dermat., Strasbourg)* **38**:563 (April) 1931.

25. Gerota, D.: Die Lymphgefäße des Rektums und des Anus, *Arch. f. Anat. u. Physiol.*, 1895, p. 240; cited by Bloom.<sup>30</sup>

26. Nesselrod, J. P.: Demonstration of Genito-Ano-Rectal Lymphatics, *Tr. Am. Proct. Soc.* **36**:85, 1935.

27. Barthels, C., and Biberstein, H.: Zur Aetiologie der "entzündlichen" Rektumstrikturen (Lymphogranulomatosis inguinalis als Grandkrankheit), *Beitr. z. klin. Chir.* **152**:161, 1931; cited by Bloom.<sup>30</sup>

mainly to the iliac and hypogastric glands, while some pass directly to the anorectal glands. The lymph vessels of the uterus go directly to the preaortic and sacral glands. Lymph glands which leave the rectal wall above the insertion of the peritoneum flow to the mesorectal lymph glands and to the glands of Gerota. Many lymph vessels lead posteriorly through the fascia of the rectum to the rectal wall, to the anorectal glands of Gerota or to the superior hemorrhoidal vessel. Lee and Staley<sup>28</sup> have two excellent drawings modified from Barthels and Biberstein illustrating the lymph pathways. Barthels and Biberstein have pointed out that the virus of lymphogranuloma venereum is able to produce a proliferation stimulus in the surrounding tissues.

Roegholt<sup>29</sup> has shown that in women there are few anastomoses between the right and left sides and between the superficial and deep lymphatic vessels; he noted that chronic lymphostasis leads to a disturbance in nutrition in the affected regions.

Bloom,<sup>30</sup> in his splendid review of the literature, concluded that obstruction of the lymph pathways leading to the inguinal glands causes a diversion of the lymph stream toward the rectum, and thus the infection is shunted to Gerota's glands.

Fischer and Schmidt-La Baume<sup>31</sup> considered that stricture results in women from infection of the vaginal mucosa, because the deep and posterior sections of the vagina send lymph into the ramified network of the pelvic lymph glands in the adipose tissue behind the rectum upward along the superior vessels and laterally along the middle hemorrhoidal vessels into a group of glands at the bifurcation of the iliac arteries.

Schreiner-Beinert<sup>32</sup> was of the opinion that women are more susceptible to inflammatory strictures, owing to the fact that conditions in the female pelvis are more favorable for infections normally because of menstruation, pregnancy and trauma resulting from childbirth. He stated that women have a greater tendency to ulcers in the rectum due to impacted feces in cases of constipation, and he also pointed out that in women there is a connection between the vaginal plexus and the hemorrhoidal plexus through the pudendal veins, so that infectious material usually passes from the vulva to the rectum.

28. Lee, H., and Staley, R. W.: Inflammatory Strictures of the Rectum and Their Relation to Lymphogranuloma Inguinale, *Ann. Surg.* **100**:486 (Sept.) 1934.

29. Roegholt, M. N.: Das genito-rectale Syndrom, *Klin. Wchnschr.* **8**:1084 (June 4) 1929; cited by Bloom.<sup>30</sup>

30. Bloom, D.: Strictures of the Rectum Due to Lymphogranuloma Inguinale, *Surg., Gynec. & Obst.* **58**:827 (May) 1934.

31. Fischer, A. W., and Schmidt-La Baume: Rektalstrikturen und Lymphogranuloma inguinale, *Deutsche med. Wchnschr.* **58**:527 (April 1) 1932.

32. Schreiner-Beinert: Ueber entzündliche Strikturen des Rektums, *Deutsche Ztschr. f. Chir.* **228**:105, 1930.

Trauma during coition has been stated by some to be one of the predisposing factors in the production of rectal strictures, and it probably is a minor factor in cases in which there is a pronounced malproportion between the size of the penis and that of the vagina; unusually vigorous coitus, according to the tilt of the female pelvis, may produce in some cases irritation of the rectum through the rectovaginal septum, at the site where strictures are most commonly found. Trauma during childbirth, however, cannot seriously be considered a major causative factor, because rectal stricture in the absence of lymphogranulomatous infection is unknown among multiparous Negro women, although they do have as a racial group a greater tendency toward keloid formation than other races.

Feilchenfeld<sup>33</sup> stated that "genito-rectal elephantiasis can be sufficiently explained by the changes in the lymph system, but for rectal strictures, local ulceration and formation of scars must be adduced. The cause of all these changes is the virus of lymphogranulomatosis inguinale."

Most authors are of the opinion that a determining factor in the production of rectal strictures is a resultant disturbance in the lymphatic flow produced by the infection.

From the foregoing and our own observations it is reasonably clear that lymphostasis plays an important part in the pathogenesis of rectal strictures in three ways: (1) blockage of lymph glands and interference with adequate drainage; (2) involvement of the lymph channels themselves, due to the action of the virus, and (3) a specific scar tissue-producing action of the virus. Sufficient evidence has not yet been produced as to why the condition in some instances is progressive to the point where it threatens life itself; in other instances why it progresses up to the point where it becomes a serious clinical problem of importance but ceases to progress beyond this point and, finally, why in some instances it is a relatively benign chronic disease. Our opinion is that these features can be explained, in the light of our present knowledge, only on the basis of the action of different strains of the virus and the reaction of the particular host. Thus it appears that one strain of the virus may be extremely pathogenic and another strain relatively benign. Unquestionably, in many persons infected with the virus clinically important manifestations of the disease never develop. On the other hand, the disease may develop in a person, produce a rectal stricture up to a certain point and never go beyond that point, and all signs of the progression of the disease spontaneously cease. In other instances the disease progresses, and in spite of all known methods of

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33. Feilchenfeld, H.: Zur Aetiologie der Elephantiasis vulvae, ano-rectalis mit den Rectumstrikturen unter besonderer Berücksichtigung der Lymphogranulomatosis inguinalis, *Med. Klin.* 28:965 (July 8) 1932.

treatment this progress is continued and ultimately produces death. The complex reactions involved between different strains of the virus and the immunity reactions of the host are facts still to be elucidated.

#### PATHOLOGY

The stricture is usually cylindric in shape, and its length varies. Oftenest it is located 2 to 4 cm. above the anus, and its length varies from 1 to 5 cm. Hartmann found the stricture in four instances 8 to 9 cm. from the anus, and he found two coexisting strictures, one at 4 and one at 12 cm. above the anus. Ordinarily it appears as a sort of funnel, with the opening at the apex of the funnel, and the opening varies in size. On proctoscopic examination ulceration may be noticed on the surface of the stricture. At the point of stricture the rectal wall is usually grayish in appearance and rigid, if the stricture is well advanced, while in the early stages it exhibits reddened granulomatous patches and often congestion and edema.

Gosselin<sup>34</sup> and, later, Fournier have described an ulceration above the stricture, which spreads circularly around the rectum and extends upward from 5 to 10 cm. and over. Above this ulceration the mucosa takes on a normal appearance. The rectal wall is thickened at the point of stricture, and all its coverings are blended into a scleroedematous mass which involves the muscular layer; oftentimes there is a great amount of scar tissue external to the muscularis. Sometimes there is a lipofibro-sclerotic change in all the walls of the rectum. Fissures and condylomas around the anus are common. Perianal fistulas are not unusual. Often they extend into the vagina or the vulva. Microscopically, the muscularis undergoes degeneration and becomes replaced by scar tissue, a subacute inflammatory process, which, according to Renard, one of Hartmann's pathologists, spreads between the normal elements of the tissue, following the vascular and lymphatic systems, compressing and destroying them. Masses of purulent exudate are present, with polynuclear leukocytes, debris of epithelial cells, red cells and clusters of bacteria. The submucosa is destroyed, and in it one finds round cell infiltrations. Deeper there are areas of round cell infiltrations, groups of polynuclear leukocytes, eosinophils, mast cells and many plasma cells. Nodular masses, which are often felt on palpation, are composed chiefly of round cells and have a center which often softens and takes on all the appearance of tuberculosis. Palisade formation is not unusual, and this feature is used by most modern pathologists as a basis of diagnosis. In short, the appearance is that of a chronic granuloma of the rectum, which for a long time was considered to be tuberculous or syphilitic.

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34. Gosselin, L.: *Recherches sur les rétrécissements syphilitiques du rectum*. Arch. gén. de méd., Paris 2:666, 1854; cited by Hartmann.<sup>10</sup>

Jeffries, who was Tuttle's pathologist, described at the same time the French pathologists did that there was a destruction of the cylindric epithelial layer and that this was replaced by striated pavement epithelium.

Diffuse sclerosis of the submucosa, with amalgamation of all the coats of the bowel, decreased the number of blood vessels, but there were no changes in the arterial walls. The normal elements of the anal wall and the perineum and the fibers of the levator ani become thin or thinned out and lose their origin, and degeneration is manifest. Hartmann pointed out that a sclerolipomatous change takes place in the perirectal tissues and that the inflammation may spread to the pelvic part of the peritoneum, giving rise to adhesions in the pouch of Douglas.

A rectal biopsy specimen shows inflammatory tissue with many epithelioid cells in palisade formation, much increase in collagen fibrils and oftentimes giant cells and eosinophils. The palisade formation of the epithelioid cells may simulate a tubercle.

The pathologic changes of the disease, aside from the gross evidence of stricture of the rectum, consist, in its early stages, of a reddened friable mucosa which bleeds easily on touch or proctoscopic examination and which is due to thickening and ulceration. The thickening involves all layers of the rectal wall—the mucosa, submucosa and tunica. Oftentimes the three layers are fused into a hard and thickened, dense mass, in which the normal histology of the rectum is lost. The scar tissue extends deeply into the adjacent perirectal tissues, and if fistulous formation is present the scar tissue extends along the tract or tracts to the external surface of the body.

All fistulas are distal to the stricture. Proximal to the stricture there is ulceration and dilatation of the rectum or sigmoid in proportion to the degree of stenosis, with a superimposed, mixed secondary infection. The obstruction to the fecal outflow plus the secondary infection is the cause of many of the secondary symptoms presented by the patients, namely, low grade fever, constipation, anemia, weakness, dehydration and malnutrition.

Hartmann reported 15 cases in which the stricture involved the entire rectum. Sometimes the area above the stricture produces a red wine color and at other times a reddish yellow. This is due to superimposed secondary infection. In the anus the papillae swell, the derma becomes infiltrated and edematous skin tags, anal fissures, sinuses, fistulas and perianal granuloma occur.

Gypstein<sup>35</sup> was the first to note that a stricture of the rectum is uniform throughout its entire length and that there are no bands or valves present.

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35. Gypstein, F.: Des effets d'électrolyse circulaire négative dans les rétrécissements fibreux du rectum, Thesis, Paris, no. 438, 1909-1910.



The rarer types of pathologic changes above the rectosigmoid are indicated in table 4. For example, Spiesman, Levy and Brotman reported a case which at autopsy showed lymphogranuloma venereum which involved the terminal part of the ileum and colon as well as the rectum.

An unusual but interesting case of fatal peritonitis from proctosalpingostomic fistula complicating a rectal stricture has been reported, with autopsy findings, by Pearce, Bower and Burns,<sup>36</sup> from the Philadelphia General Hospital. A brief abstract of the necropsy is as follows:

Bilateral, moderate hydrothorax and pleural adhesions of the left upper lobe were present. Both lungs were markedly edematous and a small embolus was evident in the right lower lobe. The heart demonstrated acute toxic degeneration. There was diffuse fibrino-purulent peritonitis. Right adnexae were absent. The spleen showed moderate pulpitis. The kidney and liver revealed acute toxic degeneration. The adrenals had lipid depletion. The pelvic veins showed thrombosis. Old adhesions of the uterus and left adnexae were present. The rectum revealed advanced lymphogranuloma with a stricture two inches above the skin margin. Careful dissection demonstrated a fistula between the left side of the rectum, just above a stricture, and the left Fallopian tube near the ampulla. . . . The uterine end of the tube was occluded.

Rectal contents passed through the open end of the tube into the peritoneal cavity. This case proves conclusively that fistulas may occur above the site of stricture, although the usual site is below.

In all cases the degree of stenosis is in direct proportion to the amount of fibrosis and inflammatory reaction present.

Mathewson is the sole observer who was of the opinion that ulceration occurs only below the stricture, and this he admitted is difficult to explain, whereas Hartmann and others, including ourselves, have noted ulceration above the site of stricture. Mathewson assumed that the perirectal glands break down to form fistulas emptying into the rectum or perirectal tissue. He was also of the opinion that the inflammatory process seen in association with venereal lymphogranuloma does not subside after colostomy, as do infections which follow carcinoma or injuries to the bowel, while Woods and Hanlon stated that "colostomy has not been used with constant success in arresting the progress of the disease." The fact is that colostomy does cause the secondary infection to subside in some instances but is, in other instances, without effect on the progress of the virus infection, which explains the two views.

Responsible observers still differ as to the actual way in which the initial lesion in the rectal mucosa begins in women. From the evidence at hand, in women one cannot say whether the process begins primarily in the mucosa, as a result of lymphatic drainage from the site of virus

36. Pearce, A. E.; Bower, J. O., and Burns, J. C.: Fatal Peritonitis from Proctosalpingostomic Fistula Complicating Lymphopathia Venereum, *Am. J. Surg.* 69:406 (Sept.) 1945.

entrance—although probably such is the case—and that the inflammation extends from the mucosa outward through the submucosa, muscularis and into the perirectal tissues or whether the process is a result of an extension from the perirectal tissues into the mucosa from without in. Some years ago one of us (L. T. W.) examined at autopsy the rectums of 18 women who had a positive Frei reaction, in the hope of adding light on this point, but none of these women showed any evidence of rectal involvement, and it was decided that this line of study was fruitless. It is our opinion, however, in the light of the frequency of proctitis without stricture of the rectum, that the virus in women is carried via the lymph channels directly to the mucosa and submucosa

TABLE 3.—*Classifications of Rectal Strictures by Different Authors*

| Grace *                        | Peyton †                                  | Sénèque ‡   | Bensaude and Lambling <sup>15</sup>  | Bacon §                            | Spicsman, Levy and Brotman #   |
|--------------------------------|---|---|--|------------------------------------|--|
| 1. Stricture with proctitis    | 1. Anal stricture                         | 1. Pure stricture limited to rectum                     | 1. Rectal stricture associated with an inguinal bubo   | 1. Stricture (alone)               | 1. Prestricture stage  |
| 2. Stricture without proctitis | 2. Rectal annular (also linear) stricture | 2. Rectal stricture with elephantiasis of external part | 2. Rectal stricture associated with edema of the labia majora                                    | 2. Stricture and esthiomene        | 2. Rectal stricture (uncomplicated)  |
| 3. Proctitis without stricture | 3. Rectal tubular stricture               | 3. Rectal stricture complicated with fistulas           | 3. Rectal stricture associated with inguinal bubo and edema of the labia majora                  | 3. Esthiomene (alone)              | 3. Rectal stricture with anal growths or anal tags (cockcomb growths)      |
|                                | 4. Rectal communicating stricture         | 4. Rectal stricture with pelvic cellulitis              | 4. Simple rectal stricture with the external manifestations in the genitalia or in the ganglions | 4. Abscess and fistulas (multiple) | 4. Rectal stricture with sinuses, fistulas or granulomas ("watering pots") |
|                                |   |   |  | 5. Postanal infection              | 5. Rectal stricture with elephantiasis, anal growths, sinuses (esthiomene) |
|                                |   |   |  | 6. Ulcerative proctocolitis        | 6. Rectal stricture with pelvic pathologic conditions                      |
|                                |   |   |  | 7. Anal stenosis                   | 7. Stricture of the entire colon   |
|                                |   |   |  |                                    | 8. Rectal stricture with associated complications                          |

\* Grace, A. W.: J. A. M. A. 122: 74, 1943

† Peyton, T. R.: Am. J. Syph., Gonorr. & Ven. Dis. 24: 360, 1940.

‡ Sénèque, J.: Bull. et mém. Soc. nat. de chir. 59: 1233, 1933; Presse méd. 42: 376, 1934; cited by Cole, H. N.: J. A. M. A. 101: 1069, 1933.

§ Bacon, H. E.: Am. J. Digest. Dis. & Nutrition 2: 570, 1935.

# Spicsman, M. G.; Levy, R. C., and Brotman, D. M.: Am. J. Digest. Dis. & Nutrition 3: 931, 1937.

themselves at the same time it is carried to the perirectal glands and tissues. The factor or factors that cause it to develop in these locations require further study. In the few women who have been passive partners in coitus per anum and in male pederasts, the problem is clear, namely, that there is a direct deposition of the virus on the mucosal wall and the process extends from within outward. In spite of the opinion of many important students of this disease, we believe that sodomy is a negligible factor in the production of stricture in women. It is hoped that further pathologic studies will clear up this point.

In table 3 we have listed the classifications of rectal strictures by different authors for purposes of comparison. Each of the classifications is of value within certain limitations, but, as our knowledge of the disease has grown, we have found that they were inadequate for purposes of a complete clinical understanding of the disease. The classification shown in table 4 was devised by one of us (L. T. W.) as an aid to a better understanding of the clinical problems involved.

TABLE 4.—*Classification of Rectal Strictures*

## I. Prestenotic proctitis

|   |   |  |   |   |   |
|---|---|--|---|---|---|
| II. Strictures:<br>types*:<br>(1) soft,<br>regular;<br>(2) hard,<br>irregular;<br>(3) firm,<br>regular;<br>(4) scir-<br>rhous | A. Simple<br>(pure or<br>limited);<br>may be<br>grades 1, 2,<br>3, 4 or 5†  | 1. Anal  | (a) Annular<br>(diaphrag-<br>matic)   | (1) Single<br>(2) Multiple  | (a) Lower rectum<br>(b) Midrectum<br>(c) Rectosigmoid |
|   |   | 2. Rectal  | (b) Tubular   | (1) Limited to a portion of<br>rectum<br>(2) Massive (diffuse) (entire<br>rectum) |   |
|   | B. Combined (with<br>other pathologic<br>conditions or<br>"complications,"<br>with associated<br>lesions and may<br>involve any of<br>organs as shown<br>in simple<br>strictures);<br>may be grades<br>1, 2, 3, 4 or 5†<br>for rectum | 3. Colo-<br>rectal   | (a) Rectosigmoid<br>(b) Sigmoid (pure or alone)<br>(c) Rectum, sigmoid and descending colon<br>(d) Rectum and entire colon  |   |   |
|   |   | 4. Ilco-rectal   | (a) Rectum and ileum  |   |   |
|   |   | 1. Local lympho-<br>granulomatous<br>lesions   | (a) Bubo (inguinal adenitis)<br>(b) Anal tumors and papillomas<br>(c) Elephantiasis<br>(d) Fistulas: (1) rectal<br>(2) rectovaginal<br>(3) proctosalphigostomic<br>(e) Pelvic peritonitis—parametritis<br>(f) Diverticulosis<br>(g) Megacolon<br>(h) Osteomyelitis<br>(i) Urethral stricture (male and<br>female) |   |   |
|   |   | 2. Carcinoma of: (Usually<br>anal; often super-<br>imposed on lympho-<br>granuloma venereum) | (a) Anus<br>(b) Rectum<br>(c) Vulya<br>(d) Abdominal wall   |   |   |
|   |   | 3. Infections (local<br>and general)   | (a) Syphilis<br>(b) Gonorrhea<br>(c) Chaneroids<br>(d) Tuberculosis   |   |   |

\* Type 1 is soft, smooth and regular due to mucosal edema and congestion; type 2 is hard and irregular, with granulomatous deposits in the mucosa and submucosa; type 3 is small amount of scar tissue in the submucosa and muscularis, and type 4 is dense scar tissue in all layers of the rectum and perirectal tissues.

† Measurement by means of bougies or rectal dilators; grade 1 admits  $1\frac{1}{2}$  inch (3.7 cm.); grade 2 admits 1 inch (2.5 cm.); grade 3 admits  $\frac{1}{2}$  inch (1.2 cm.); grade 4 admits  $\frac{3}{4}$  inch (0.6 cm.), and grade 5 admits none.

Marino<sup>37</sup> used the proctoscope as a means of measuring stricture lumens. The diagnosis in cases of pure uncomplicated strictures of the rectum is made by means of the examining finger. External manifestations of the disease in all cases demand a rectal examination.

37. Marino, A. W. M.; Buda, A. M.; Turell, R., and Nerb, L.: The Treatment of Venereal Lymphogranuloma with Sulfanilamide, *Am. J. Surg.* **46**:343 (Nov.) 1939. Marino, A. W. M.: The Anorectal Aspect of Venereal Lymphogranuloma, *ibid.* **45**:293 (Aug.) 1939.

Obvious stigmas of strictures of the rectum make the diagnosis easy if the patient presents elephantiasis of the vulva (figs. 4 and 5), anal tags (fig. 1), fistulas, fissures, cockscomb tumors (fig. 2) or papillomatous tumors around the anus which are obviously of a benign nature. The



Fig. 1 (patient S. A.).—Anal edema with tags. Stricture of the rectum of six years' duration.

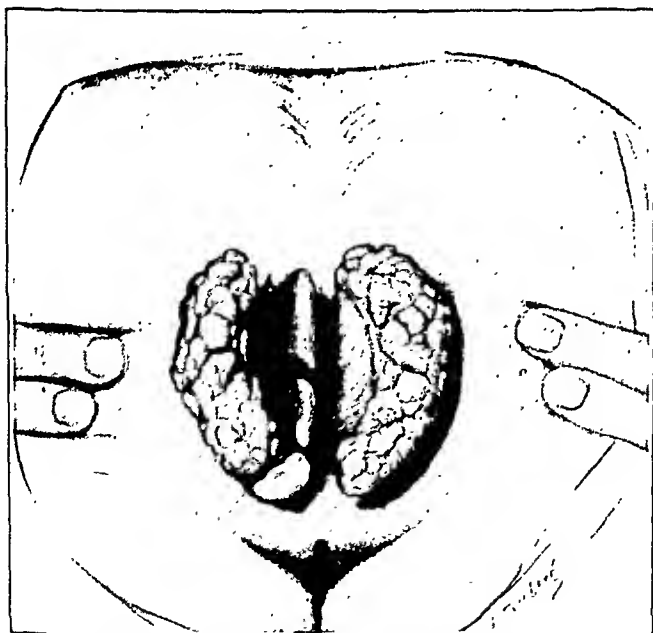


Fig. 2 (patient M. B.).—Artist's drawing of cockscomb growth, showing anal tumor, stricture of the rectum and fibroid of the uterus. A photograph of this tumor was published by us in a previous paper.<sup>10</sup>

reason for this is that practically all physicians today make a rectal examination in such cases. Incidentally, these tumors may grow to

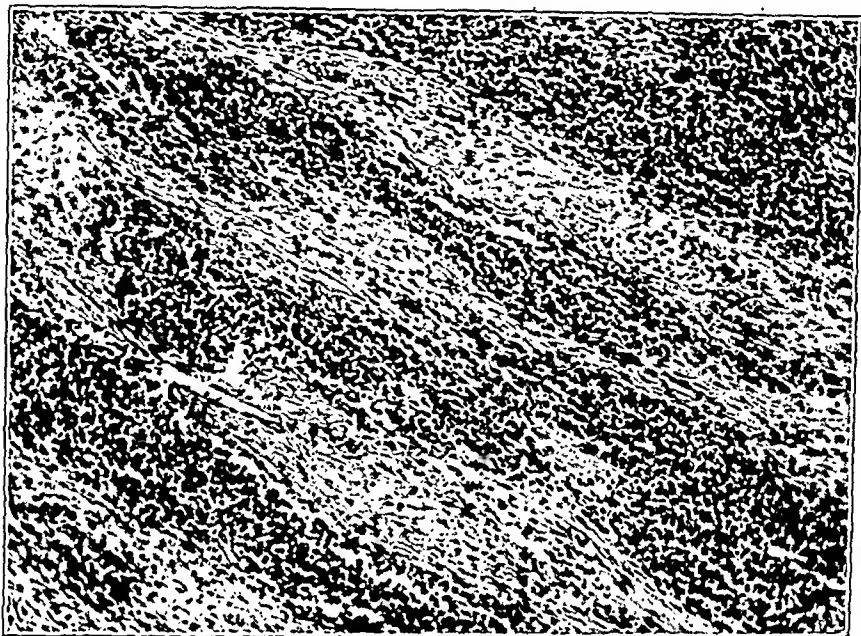


Fig. 3 (patient M. B.).—Photomicrograph of sections taken from the anal tumor, showing bands of lymphocytic infiltration among bands of fibrous tissue.

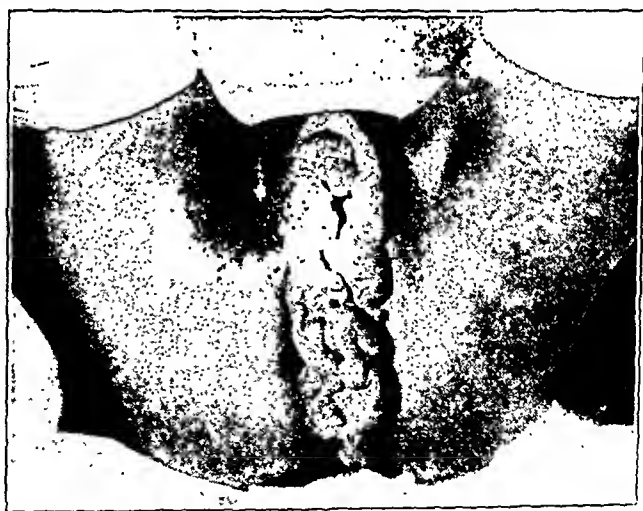


Fig. 4 (patient T. S.).—Multiple tumors involving the labia majora and minora, perineum and anus, with stricture of the rectum. The condition began eighteen years before this article was written. Edema is slight or absent.

the size of one's fist. Cryptitis is often present. Fistulas with a growth of granulation tissue around the fistulous opening or openings are not uncommon. At times there is a simple rectovaginal fistula, but we

have seen cases in which the rectovaginal septum has been almost completely eroded or destroyed near the anus and also involved the perineal muscles.

In a few cases there is a phagedenic ulcer that extends from the anus into the vagina, destroying the perineal body; sometimes these ulcers have hard edges. Often in such cases there is a superimposed anal carcinoma or cancer occurring in association with the lymphogranulomatous condition. Liccione<sup>38</sup> was the first to point out the coexistence

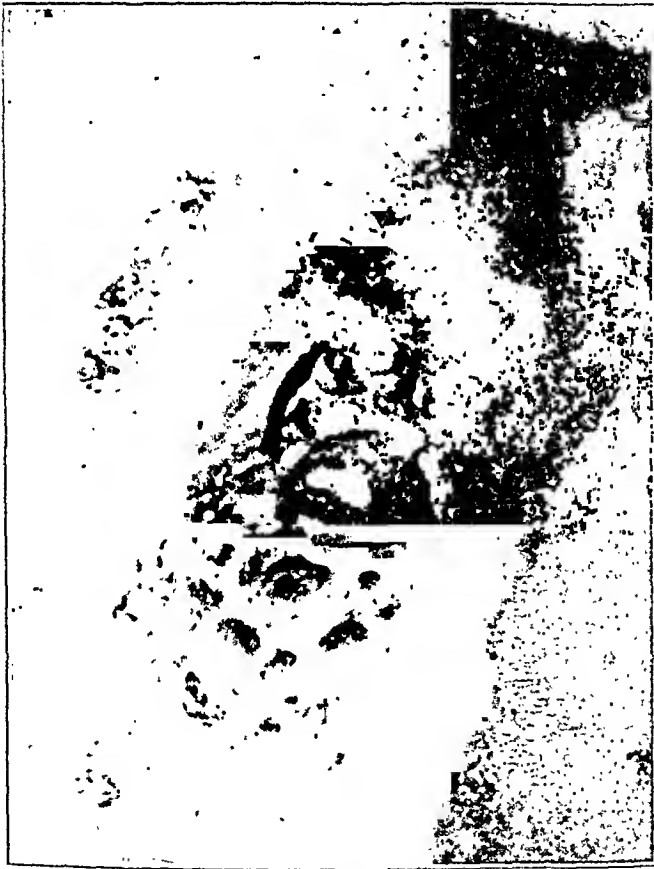


Fig. 5 (patient S. D.).—Elephantiasis of the vulva and clitoris, with massive tumor of the right labia minora with stricture of the rectum. The tumor was extirpated, and abdominoperineal resection of the stricture was done. Squamous cell carcinoma of the left edge of the vagina and rectum developed. The carcinoma was treated with radium. Several weeks later there developed numerous sinuses discharging pus from an ulcer of the left side of the vagina and upper part of the left leg. The patient died; autopsy was not done. The photograph was secured through the courtesy of Dr. M. E. Ross, with whom the senior author saw the patient in consultation. The case was described in detail in a previous article by us.<sup>16</sup>

38. Liccione, W. T.: Venereal Stricture of Rectum: Adenocarcinoma as a Late Complication of Lymphogranuloma Inguinale, *Am. J. Surg.* **31**:551 (March) 1936.

of carcinoma and rectal strictures. Carcinoma of the rectum sometimes produces a stricture which simulates stricture due to lymphogranuloma venereum.

In 27 cases in this series the diagnosis of rectal stricture was first made in our obstetric service after the patient was admitted to the hospital in labor by the obstetrician who made a rectal examination on these patients. They were patients who had failed to visit the prenatal clinic.

In most cases rectal examination shows the rectal wall to be thickened and narrowed. The lumen may admit the tip of the index finger, or there may be almost complete occlusion, which will barely permit the passage of a ureteral catheter.

The diagnosis may be confirmed by proctoscopic examination if an anal stricture does not preclude the use of a proctoscope.

Our records show that the Frei test was performed many times in cases in which, unfortunately, they were not recorded. Of 118 cases, it was positive in 91, or 77.1 per cent, and negative in 27, or 22.9 per cent. In some instances the original Frei antigen was used, in some the mouse brain antigen was used and at present we are using the chick embryo antigen.<sup>39</sup> Although an important adjunct in the diagnosis of the disease, the Frei test is not absolutely specific and negative reactions occur in a sufficient number of cases for us not to place the absolute reliance on the test that we would have a few years ago. Some negative reactions to the Frei test were undoubtedly due to faulty technic in the performance of the test, because in many instances positive reactions have been obtained when a retest was insisted on. It should, however, be done in all cases of suspected strictures, and when positive it is a most important confirmatory diagnostic aid. If negative, it is important to repeat the test with potent antigen and scrupulously careful technic. The cultivation of the virus from the rectal mucosa obtained from the site of the stricture, of course, makes the diagnosis absolute.

Hyperproteinemia with a definite increase in serum globulins in excess of 3.5 per cent in lymphogranuloma venereum was first noted by Gutman.<sup>40</sup> It is a suggestive diagnostic sign that has been confirmed by us. The reversal of the albumin-globulin ratio in early and late cases, which persists as long as any active infection remains, is stressed by Howard, Eisenman and Strauss.<sup>41</sup> We have found it to be present in all cases, with the condition active or otherwise, during the past six

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39. Lygranum, as kindly supplied us by E. R. Squibb & Sons.

40. Gutman, A. B.: Systemic Manifestations of Lymphogranuloma Venereum, New York State J. Med. **39**:1420 (July 15) 1939.

41. Howard, M. E.; Eisenman, A. J., and Strauss, M. J.: Alterations in the Serum Proteins in Lymphopathia Venerea, Am. J. Syph., Gonorr. & Ven. Dis. **23**:83 (Jan.) 1939.

months. Gutman considered hyperproteinemia as a reflection of the immune response of the organism to the infection. The sedimentation rate has not been a diagnostic help in these cases.

The anemia and amyloid changes are those found in all chronic diseases and are not specific.

Biopsy should be used in two ways: (1) to rule out the presence of a coexisting carcinoma as a result of histologic study, although the presence of carcinoma should not prevent one from attempting to isolate the virus, because carcinoma is often superimposed on lymphogranuloma, and (2) to isolate the virus in institutions where laboratory facilities make this procedure possible, and it is our opinion that it will be increasingly used. In this series of cases biopsies were done in 34 instances, but virus isolation studies were not done, although at the present time we are undertaking this method of study.

TABLE 5.—*First Symptom in 461 Cases*

| First Symptom  | Cases, No. |
|--|------------|
| Constipation .....   | 172        |
| Rectal bleeding .....  | 49         |
| Alternating constipation and diarrhea .....                                    | 40         |
| Ribbon stools (narrowed, thin or pencil-like) .....                            | 39         |
| Anal fistulas .....  | 36         |
| Abdominal pain (without other obstructive symptoms) .....                      | 24         |
| Colostomies .....  | 24         |
| Purulent discharge .....   | 23         |
| Acute intestinal obstruction (pain and vomiting) .....                         | 23         |
| Pain on defecation .....   | 12         |
| Diarrhea .....   | 11         |
| Pruritus ani .....   | 4          |
| Abdominal catastrophe (rupture of rectum following dilatation in clinic) ..... | 4          |
| Total .....  | 461        |

The Wassermann test was carried out and recorded in 287 cases, the reactions in 91, or 31.4 per cent, being positive and in 196, or 68.6 per cent, negative. At the present time the Frei test is routinely done on all patients in our proctology clinic, as is a Wassermann test. In some instances we do a complement fixation test for lymphogranuloma, although the patient may not have any suggestive symptoms of the disease.

In table 5 we have listed the leading symptoms in 461 cases. From that table it is seen that constipation, rectal bleeding, alternating constipation and diarrhea and ribbon stools occur most frequently. In 5 patients in this series the diagnosis was made of ulcerative colitis.

In table 6 we have recorded the lesions combined with strictures of the rectum.

The location of the stricture was definite in 182 cases, as shown in table 7, which is a fairly representative average percentage for the entire series.



The signs and symptoms obviously vary according to the location and degree of the stricture. (See figs. 6, 7 A, 8 and 9.)

Some patients have come to the hospital with pneumonia, and the stricture of the rectum was an incidental finding. Fibroids are frequently found in association with lymphogranuloma. Tuberculosis is a frequent concomitant infection in this disease. Many of the patients come into the hospital during an acute episode, with either abdominal pain, vomit-

TABLE 6.—*Lymphogranulomatous Lesions Associated with Rectal Strictures*

| Lesion  | Cases, No. |
|---|------------|
| Anal fistulas .....   | 53         |
| Rectovaginal fistulas .....   | 34         |
| Perianal tags or cockscomb growths.....                                   | 22         |
| Hemorrhoids .....   | 17         |
| Elephantiasis of the vulva (esthiomene).....                              | 11         |
| Carcinoma .....   | 6          |
| Arthritis .....   | 4          |
| Osteomyelitis .....   | 4          |
| Pelvic peritonitis .....  | 3          |
| Elephantiasis of penis or scrotum and stricture of urethra                | 1          |
| Ovarian tumor (pathologic examination showed to be lymphogranuloma) ..... | 1          |
| Total.....  | 161        |

ing, pain in the rectum or constipation, and, as soon as the acute episode has passed, in one or two days, they leave the hospital without permission; this necessarily makes the hospital records incomplete, because the patients do not remain sufficiently long to be properly studied.

It has been hard for the patients to determine the exact time of onset of the stricture. One third of the patients stated that it had been of one year's duration, another third stated that it had been of two years'

TABLE 7.—*Location of the Stricture*

| Location                                       | Cases, No. |
|--|------------|
| Lower part of the rectum involved.....         | 138        |
| Entire rectum involved.....                    | 30         |
| Sigmoid involved .....                         | 8          |
| More than one stricture, different levels..... | 6          |
| Total.....                                     | 182        |

duration and in the remainder of our cases it varied up to twenty-two years or more.

Seventy-seven women in this group of cases had children before they were aware of the fact that they had a stricture, and 22 women in this series have borne children after the diagnosis of stricture was made. It is clear, therefore, that lymphogranuloma per se does not preclude the possibility of pregnancy, although there is some evidence that infected women are not so fertile as those without the infection.

Kassebohn and Schreiber were the first to report rupture of the rectum caused by rectal stricture during childbirth. Subsequently, they reported 18 cases of rectal stricture at childbirth at full term from the



Fig. 6.—*A*, roentgenogram of barium enema in patient L. J. There was a stricture of the rectum 2 inches (5 cm.) from the anus. *B*, roentgenogram of barium enema in patient R. E. The stricture of the anus was of five years' duration. No previous operation was performed.



Fig. 7.—*A*, roentgenogram of barium enema in patient F. J. A stricture of the rectum and sigmoid with multiple anal fistulas was present. *B*, roentgenogram of rectal stricture with numerous draining sinuses in patient A. T.

obstetric service at Harlem Hospital. They advised therapeutic abortion if the presence is discovered early, and in cases in which this is impractical (the religious viewpoint may enter) pregnancy may be permitted to proceed, with an attempt at spontaneous delivery or cesarean section, but in no circumstances should instrumental delivery be attempted.



Fig. 8 (patient E. H.).—Roentgenogram of barium enema. There was a stricture involving the entire rectum, with a fistula in ano.

#### LABORATORY FINDINGS

The most constant finding has been low grade secondary anemia. The red cell count has averaged between 3,500,000 and 4,000,000. Many patients showing a count of 4,000,000 cells were so dehydrated that hemoconcentration had to be taken into consideration. The white cell count showed no special change except during crises of one type or another. Urinary findings have been, on the whole, normal. One patient in this series had diabetes. Urea nitrogen and creatine levels, blood sugar content and blood chloride levels were, on the whole, usually normal. The sedimentation rate, on the whole, was normal, except in the presence of pronounced secondary infection. Determinations of blood fibrinogen were made in about 30 of these cases, and they were within normal range.

## ROENTGENOGRAPHIC EXAMINATION

Barium enemas have been used in over 100 of these cases, and they demonstrated the presence of stricture. It is invaluable in cases of high stricture (fig. 11 *A*) because only through its use can information be obtained as to the underlying pathologic changes. One disadvantage of the barium enema is that in narrow strictures the barium may become inspissated and thus at times aggravate the clinical condition of an extremely sick patient. In low strictures, we have used, with success, a balloon passed through the stricture, and it is then filled with sodium iodide and the roentgenogram taken (fig. 9). This has given us accurate information as to the length of the stricture, without any of the disadvantages from inspissation of the barium when used as an enema. In acute intestinal obstruction superimposed on the chronic obstruction



Fig. 9 (patient C. J.).—Roentgenogram of a rubber balloon introduced through the stricture and filled with sodium iodide solution. This shows the stricture of the lower one half of the rectum. It indicates the ease with which, in selected cases, this technic is used and that it is preferable to that of a barium enema. There is no inspissation of the barium above the site of the stricture.

that is present in these cases, flat roentgenograms show distention of the large bowel and, in some instances, distention of the small intestines, with fluid levels.

## DIAGNOSIS

The diagnosis is relatively simple if the stricture is located low in the rectum. The chief point to remember is that a rectal examination should be made in any patient presenting symptoms of constipation, deformed or ribbon-like stools, hemorrhage per rectum or a discharge of pus per rectum. Elephantiasis of the vulva or scrotum or anal tags are only additional clues which indicate that a rectal examination should be made. Proctoscopic examination is sometimes valuable in confirming

the diagnosis. Proctoscopy and sigmoidoscopy are helpful if the lesion is in the rectum or rectosigmoid areas. Care must be used in making a proctoscopic examination, because of the danger of rupture of a diseased rectal wall. The Frei test, the complement fixation test and the albumin-globulin ratio are valuable diagnostic aids. Roentgenologic examination is important in strictures that are above the reach of the finger or the proctoscope. Biopsy will prove the presence of granulomatous tissue, and, of course, the isolation of the virus makes the diagnosis absolute.

#### DIFFERENTIAL DIAGNOSIS

1. Intestinal tuberculosis may cause formation of strictures as a part of tuberculosis of the intestinal tract.

2. In ulcerative colitis the diarrhea, dehydration, loss of weight and anemia may cause one to consider lymphogranuloma venereum as the causative agent.

3. Carcinoma of the rectum without lymphogranuloma has to be ruled out. Liccione, however, described 2 cases of adenocarcinoma of the rectum superimposed on lymphogranuloma. Woods and Hanlon and Barber and Murphy<sup>42</sup> have each described 3 cases in their series. We have found carcinoma superimposed on lymphogranuloma in 5 instances.

4. Diverticulitis may produce any of the symptoms caused by lymphogranuloma venereum, such as diarrhea, constipation and rectal bleeding. Roentgenographic examination by means of a barium enema makes the diagnosis clear. Chronic diverticulitis can result from rectal stricture, as shown in the case of Phemister's cited by David and Lauer.<sup>43</sup>

5. Chemical strictures must be ruled out. Rosser described a chemical stricture of the rectum, which is relatively rare. The patients give a history of receiving injection treatments for hemorrhoids.

Strictures due to parasites, amebic ulcers and other conditions are so rare in this country that they need only to be mentioned.

#### PROGNOSIS

Rectal strictures due to lymphogranuloma venereum are the most serious clinical condition that results, on a large scale, from this disease. Many persons in whom strictures of the rectum develop live to a relatively extreme old age. In other instances, the stenosis of the rectum not only causes disability and prolonged morbidity, but it is

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42. Barber, W. H., and Murphy, W. B.: *Lymphogranuloma Venereum*, Ann. Surg. **113**:30 (Jan.) 1941.

43. David, V. C., and Lauer, C. A.: *Stricture of the Rectum with a Consideration of Some Unusual Causes*, J. A. M. A. **98**:1 (Jan. 2) 1932.

the real cause of death in many instances. The disease is progressive at times, oftener it is apparently static and in the present state of our knowledge it is impossible for any one to isolate with accuracy the conditions that will progress from those that will not, due to many not fully understood factors. Worth while mortality statistics cannot be produced, because of this fact and also because the patients roam from doctor to doctor and from clinic to clinic.

Tuberculosis develops as a death-producing factor in a large number of these cases. Pneumonia here in New York is a serious factor in other instances. Acute and chronic intestinal obstruction develops not infrequently. It has been stated that strictures of the rectum never cause death but are always present at the time of death. Rectal strictures are a common cause of death, but often the death-producing factor is not considered to be the stricture, because of other complications.

#### TREATMENT

Numerous methods of treatment have been used in these cases. The scope of this paper permits only a brief discussion of a few of them.

*Drugs.*—For many years fuadin was used in our clinic, without success. Shropshear<sup>44</sup> was the first to use sulfanilamide in these cases. Grace recommended sulfathiazole. Levy, Holder and Bullowa treated 120 patients in our clinic with sodium sulfanilyl sulfanilate and were impressed by the immediate results obtained. Subsequent follow-up after three years has been unimpressive. This is not taken to mean that the use of sulfonamide drugs in the prestricture stage of the disease may not in some instances prevent further progress of the condition and in this way stop formation of strictures. The cases in which this may occur we cannot state with certainty. We are sure, however, that sulfathiazole, sulfanilyl sulfanilate and succinylsulfathiazole will clear up much of the secondary superimposed infection and in this indirect way improve the condition of the patient. No evidence has been forthcoming that sulfonamide drugs are viricidal in their action. At present we are using phthalylsulfathiazole. Antimony and potassium tartrate, as recommended and used by Stone,<sup>45</sup> has proved valueless except as a mild general tonic. We have used penicillin in a few cases recently, and this has proved less successful than the sulfonamide compounds. Certain conditions will go on to serious formation of fibrous strictures

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44. Shropshear, G.: Sulfanilamide in the Treatment of Strictures of the Rectum Caused by Lymphogranuloma Venereum, Illinois M. J. **74**:153 (Aug.) 1938.

45. Stone, H. B.: Stricture of the Rectum; Carcinoma of the Rectum, J. South. Med. & Surg. **98**:1 (Jan.) 1936.

in spite of drugs in cases in which the virus shows real pathogenic activity. In patients in whom the symptoms and signs are predominantly due to congestion, edema and ulceration caused by secondary infection, sulfonamide drugs are of positive value, but they cannot and do not cure fibrous stricture of the rectum, because of (1) lack of viricidal potency and (2) poor vascularity of scar tissue, which will not permit sufficient concentration of the drug at the point where it is needed to be of effective consequence. It is obvious that drugs cannot remove scar tissue.

*Biologic Methods.*—A. Antigens: Frei antigen has been used in our clinic and in many other clinics and is still recommended by some clinicians as a method of treatment. In our clinic at least it has proved to be valueless. It has been used in over 200 cases, without effect. Seidenstein<sup>46</sup> used Frei antigen with sulfonamide drugs. Frei himself stated that the use of Frei antigen or the cutaneous test may produce an acute exacerbation of a local lesion. This we have never observed.

B. Estrogens: Seley, Vernick and Goldman<sup>47</sup> reported improvement in 4 patients treated with parahydroxyphenyl ethyl hexane, a dose of 30 mg. a day being used. The basis for the use of estrogens, as explained by them, is that pregnancy seemed to help rectal strictures by causing a softening of the genital, pelvic and perineal tissues during childbirth. Palmer, Kirsner and Rodaniche reported that pregnancy seemed to help their patients. Schreiber<sup>48</sup> denied this, and in support he quoted the statistics of our obstetric department.

C. Irradiation: We have had no experience with the use of deep roentgen therapy or of radium in these conditions, and for that reason we are unable to make a definite statement. We have had a few patients come to us having advanced strictures who had received radium therapy in other institutions. It did not seem to us that the pathologic changes or the progress of the condition had been lessened, because when we saw these patients their lesions had continued to advance in spite of their radiation therapy.

D. Diathermy: The literature is replete with reports of cases in which diathermy has softened the stricture and in some cases caused a retrogression of the stricture. Years ago, diathermy was used in the clinic of this hospital, and its results were totally unsatisfactory.

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46. Seidenstein, H. R.: Rectal Stricture Due to Lymphogranuloma Venereum: Treatment with a Sulfonamide and Frei Antigen, *Surgery* **14**:73 (July) 1943.

47. Seley, A. D.; Vernick, S., and Goldman, H.: The Estrogen Treatment of Stricture of the Rectum Due to Lymphogranuloma Venereum, *J. Clin. Endocrinol.* **5**:301 (Sept.) 1945.

48. Schreiber, M. J.: Personal communication to the authors.

E. Solid Carbon Dioxide.—Solid carbon dioxide was used, ineffectually, in a large number of cases in our outpatient department over a period of several years, and it was discarded because it served no useful purpose.

*Surgical Methods.*—A. Dilation: Dilation by finger and bougies has been widely used. Finger dilation is a safe method in conditions that are not too far advanced. It cannot be used in strictures beyond grade 3. Dilation of these strictures by means of bougies has resulted in death at times, as evidenced by the report of Woods and Hanlon of seven deaths in 192 cases. In our clinic four deaths occurred. In 1 case early operation prevented death, and in this case colostomy in the transverse colon was performed and also drainage of the abdomen after the rent in the rectum had been sutured. The use of Wales bougies and other mechanical methods of instrumental dilation has been surgery's chief weapon in its attack on this condition. The only objection to the use of bougies and other mechanical dilators is that they tear the stricture, and this increased trauma stimulates greatly the subsequent formation of scar tissue; in fact, the late condition of many of these patients is worse owing to the extra scar tissue caused by the dilation. In certain selected cases dilation is a valuable palliative method of treatment to be used with judgment by surgeons who have a thorough understanding of the pathologic changes.

B. Internal Proctotomy: Internal proctotomy, which means to divide the stricture within the rectum by means of an incision, is similar in every way to the operation of internal urethrotomy. Surgeons who advise its use maintain that the ultimate results depend on the care with which the stricture is kept dilated. We have used it in selected cases, although we were aware at the time of the fact that it was not a satisfactory definitive method of treatment, because the trauma produced by this procedure stimulated the production of more scar tissue, which after a few months made the stricture much more rigid and sometimes impassable. Internal proctotomy, in our opinion, is only a palliative method of treatment for stricture at the time when fistulas are being excised and as a part of a plan of treatment preliminary to colostomy in greatly weakened patients. This, of course, varies with the individual case, because we feel that it is better to do an internal proctotomy and give the patient temporary relief as a preliminary to other planned procedures. Most surgeons agree that internal proctotomy is not a sound method of treatment per se.

C. Complete or External Proctotomy: Complete or external proctotomy means an incision through the stricture and the posterior



commissure extending down to the tip of the coccyx, which includes throughout its entirety the anal sphincter posteriorly. Bougies have to be used after the operation. Hartmann reported that he performed sixteen such operations in 1895, and the results were unsatisfactory. This operation, as experienced in a number of cases, not only adds to the amount of scar tissue already present but greatly stimulates the subsequent cicatrix so that it is more pronounced than before. We used this operation in a number of cases some years ago, and we agree with Hartmann that it is not a curative procedure but only palliative and that the only justification for its use is a part of a plan in which subsequent corrective procedures are contemplated.



Fig. 10 (patient B. T.).—Sponantous closure of colostomy for rectal stricture. Six months after colostomy, bowel movements per rectum became normal. This shows the appearance of the colostomy six years later. Occasionally a bit of flatus passes through the colostomy. This illustrates the beneficial effects of colostomy alone in certain cases. The patient has had a course of treatment with sulfonamide drugs since the colostomy.

D. Permanent Colostomy: Permanent colostomy is the operative procedure of choice of most American surgeons. Tuttle and other earlier surgeons, as well as Mathewson, Woods and Hanlon and others, agreed that it does not stop the progress of the disease. In most instances, the patients are relieved of pain, they gain in weight and their clinical condition improves considerably. The disadvantages are (1) objection by the patient to a permanent artificial anus, (2) stricture of the colostomy opening and at times infection around the stoma, (3) anterior grade herniation of the bowel through the colostomy opening, and (4) retrograde herniation through the bowel through the colostomy opening (figs. 10, 12, 13 and 14). In some instances permanent colostomy, in which the stricture is not resectable, is the

only operation possible for the surgeon to perform, and in these cases it is life saving. A permanent colostomy is necessary in all cases in which an abdominoperineal resection of the rectum is indicated. A more detailed discussion of colostomy for rectal strictures was presented by us in a previous paper.<sup>1e</sup>



Fig. 11 (patient V. M.).—*A*, stricture of the sigmoid and rectum. *B*, mottling of the third and fourth lumbar vertebrae, indicating osseous involvement.

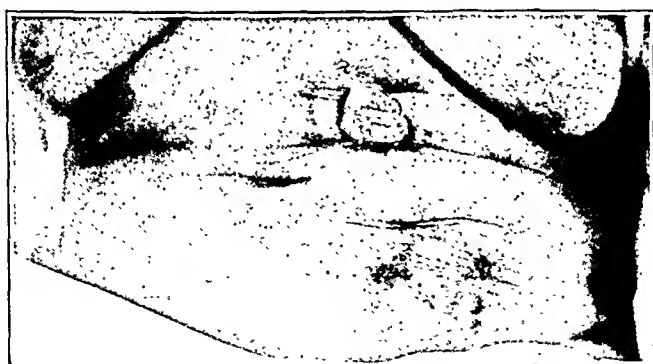


Fig. 12 (patient C. B.).—The patient, aged 60, had a rectal stricture for forty years. Left inguinal colostomy was done twenty-four years after it appeared and double-barreled colostomy one year later because the left inguinal colostomy became strictured. The second colostomy continues to function well, but discharge from the left inguinal colostomy began after fifteen years. This subsided, and the lesion healed after three weeks' treatment with phthalylsulfathiazole.

E. Warthen's<sup>49</sup> Operation. Warthen's operation is a modified permanent colostomy operation devised for patients with rectal strictures. He obliterates the cul-de-sac of Douglas by painting it with one-half strength tincture of iodine solution and then uses a series of purse string sutures of chromic surgical gut in each fossa lateral to the rectum. A double-barreled colostomy is then performed through a McBurney incision on the left. Warthen treated 10 patients in this way. The only possible advantage of Warthen's operation—and this is still to be proved—is that it may prevent anterior grade or retrograde herniation.

F. Temporary Colostomy: The chief indication for the performance of a temporary colostomy occurs in cases in which it is planned to do a resection of the rectum with preservation of the anal sphincter.



Fig. 13 (patient L. H.).—The patient had a right inguinal bubo twenty-one years before we saw her. There was a history of rectal stricture for sixteen years, foul rectal discharge with odor and rectal hemorrhages for eleven years and colostomy was done three years before this article was written because of vomiting and abdominal distention. There is massive herniation of the abdominal wall at the site of the colostomy. Scars of previous buboes are to be noted.

G. Jelk's<sup>50</sup> Operation: The operation consists of bilateral incisions up to and beyond the upper border of the stricture. The stricture is divided by turning the knife blade toward the intestinal wall, with the finger in the rectum as a guide. The mucosa is left intact. The ulcerated mucosa is treated with antiseptics. The lateral incisions are drained with

49. Warthen, H. J.: Operative Treatment for Benign Rectal Stricture (Lymphogranuloma Venereum): Preliminary Report, *Arch. Surg.* **38**:617 (April) 1939.

50. Jelk, J. L.: A New Operation for Rectal Stricture, *Tr. Am. Proct. Soc.* **32**:19, 1931.

iodoform gauze. Bacon, Murray and Schoenfeld<sup>51</sup> operated on 24 patients, and these patients were symptomatically improved. We carried out this procedure in several cases, and the results were unsatisfactory.

H. Lockhart-Mummery and Lloyd-Davies<sup>52</sup> Operation: The coccyx is removed, the postrectal fascia is divided and the rectum is drawn into the wound, which permits a longitudinal incision of the stricture. The incision is sutured transversely. In the 2 patients that we have seen on whom this operation was performed, the results were failures.

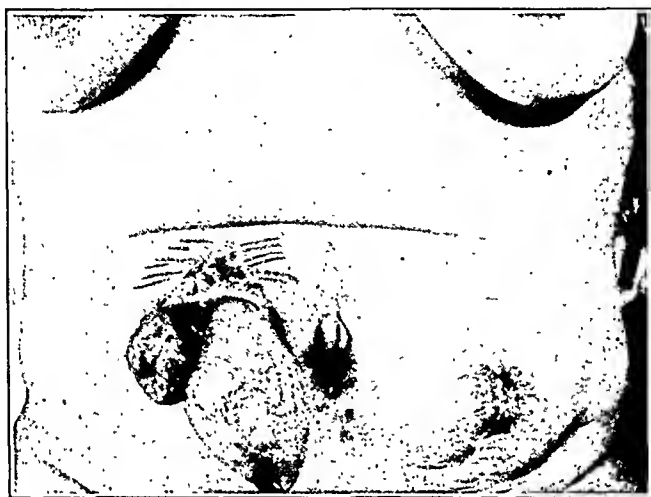


Fig. 14 (patient A. W.).—Anterior grade and posterior grade prolapse of the colostomy in the transverse colon. Left inguinal colostomy had been performed in another hospital eleven years before the patient's admission to the hospital. Right inguinal colostomy had been performed ten years later. The left inguinal colostomy is completely healed. The right rectus colostomy shows a serious degree of prolapse. With phthalylsulfathiazole as preoperative medication, the prolapsed segments of the transverse colon were resected and the patient was discharged, improved.

I. The Stone Operation: Harvey Stone divides longitudinally the posterior vaginal and anterior rectal walls, suturing the edges of the vaginal incision to the edges of the rectal mucosa. A flap on each side of the vaginal mucosa is dissected up and sutured to the midline. The free edges of the vaginal mucosa are brought together over these free

51. Bacon, H. E.; Murray, F. H., and Schoenfeld, J. D.: Rationale of Jelk's Operation for Rectal Stricture: Preliminary Report, *Am. J. Surg.* **27**:476 (March) 1935.

52. Lockhart-Mummery, J. P., and Lloyd-Davies, O. V.: The Operative Treatment of Fibrous Stricture of the Rectum with the Description of a New Technique, *Brit. J. Surg.* **23**:19 (July) 1935.

flaps, thereby grafting normal vaginal mucosa into the stricture in order to establish a lumen. Lockhart-Mummery objected to this operation because of the danger of forming rectovaginal fistulas. We have had no experience with this procedure.

J. Keller's<sup>53</sup> Tunnel Skin Graft Operation: In 1933, Keller advocated the use of tunnel skin grafts in the treatment of strictures of the rectum. Full thickness grafts are taken from a hair-free area. A trocar and cannula are passed under the stricture. The trocar is withdrawn, a cannula being left in place under the mucous membrane. The graft is attached to a black silk ligature by means of a carrier. The graft is drawn into position by the exertion of a pull on the ligature pulled through the stricture. Usually three or four grafts are placed at equal distant points. Pressure is maintained with a distended Hagner or Pilcher bag. The bowels are not allowed to move for seven days. Keller reported on 8 cases. We have found this operation to be of value only in cases of anal stricture. Most anal strictures are due to a previous operation and are not due to lymphogranuloma. In extremely low lymphogranulomatous strictures it may be of value.

K. Hartmann's Sacroperineal Operation: Hartmann reported satisfactory results with a sacroperineal operation and preservation of the sphincter in a large number of cases. Although we have had no experience with Hartmann's operative procedure, we are of the opinion, because of his great knowledge of the disease, that it is worthy of extensive investigation and trial.

L. Pauchet's<sup>54</sup> Intrasphincteric Excision Operation: This operation, which we have used in 26 cases, is an endoanal excision of the rectum, with preservation of the sphincter following, in most cases, a temporary colostomy, the healthy rectum later being brought down through the sphincter and sutured to the skin. In 2 cases we have performed this operation in one stage, but in these 2 cases the pouch of Douglas was not opened. In our hands, Pauchet's operation has proved to be a worth while and satisfactory operation, which we can recommend wholeheartedly. The operation, however, can be used only in selected cases. If the stricture extends for more than 6 inches (15 cm.) above the anus, the procedure cannot be used. It also cannot be used if the sigmoid is plastered down with adhesions within the abdominal cavity. It should be used only by experienced surgeons and then in carefully selected cases.

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53. Keller, W. L.: Annular Stricture of the Rectum and Anus: Treatment by Tunnel Skin Graft; Preliminary Report, *Am. J. Surg.* 20:28 (April) 1933.

54. Pauchet, V.: *Practical Surgery Illustrated*, London, Ernest Benn, Ltd., 1925, vol. 4, p. 195.

M. Abdominoperineal Resection Operation: Edwards and Kindell,<sup>55</sup> Barber and Murphy and Woods and Hanlon have reported excellent results from abdominoperineal extirpation of the diseased rectum and the formation of a permanent colostomy. In our opinion the indication for an operation utilizing the abdominoperineal excision is the fact that the strictured area involves the entire rectum or rectosigmoid; because of the extent of the disease it is impossible to bring down the proximal loop of bowel to the anus after the diseased area has been excised. We would add, as an additional prerequisite for such an extensive operation, that the patient should show clinical signs of disease activity of a serious nature which do not subside after a permanent colostomy.

#### ABSTRACTS OF HISTORIES IN CERTAIN ILLUSTRATIVE CASES

##### CASE 1.—*Simple stricture of the rectum; pronounced constipation.*

The patient was a Negro woman 30 years of age. There had been severe constipation, which during the past year had become progressively worse. Stools came out in thin strips and at times were streaked on the outside with bright red blood. During the past year the patient had lost 20 pounds (9.1 Kg.) in weight and had complained of vaginal discharge with itching. A rectal stricture was found 1½ inches (3.8 cm.) above the anal opening, which admitted the tip of the finger. Reaction to the Frei test was positive, and the Kahn reaction of the blood was negative.

##### CASE 2.—*Stricture of the rectum with diarrhea.*

A Negro woman 33 years of age entered the hospital with a temperature of 100 F. She had had a tooth extracted twenty days before. Eleven days before admission there developed diarrhea of five loose, watery stools per day. There was tenderness in both fornices on vaginal examination. Rectal examination revealed an annular stricture that was tender and indurated and which admitted the tip of the index finger. Proctoscopic examination revealed ulceration above the site of the stricture. With a regimen of rest and irrigations high in the colon the patient improved, and she left the hospital nine days later, without permission.

##### CASE 3.—*Stricture of the rectum with alternating constipation, diarrhea with blood and mucus in stools; colostomy.*

A Negro woman 45 years of age entered the hospital complaining of constipation alternating with diarrhea and with blood and mucus in the stools. She stated that she had lost a large amount of weight. The stools were ribbon-like in character. There were three or four perianal sinuses discharging pus about the anus. Digital examination of the rectum revealed a stricture 3 inches (7.6 cm.) above the anal orifice. Proctoscopic examination showed an area of induration and ulceration about the stricture and above the stricture. Reaction to the Frei test was positive. A biopsy specimen from the rectum showed acute inflammation. Left inguinal colostomy was performed ten days after admission. The patient was discharged three weeks later, improved.

55. Edwards, M., and Kindell, F. B.: The Treatment of Rectal Lymphogranuloma by Excision, *Surgery* 4:809 (Dec.) 1938.

CASE 4.—*Constipation and bleeding per rectum; colostomy.*

A Negro woman 33 years of age had had pain and bleeding per rectum on defecation for the past eighteen months. She had been treated in the clinic for some months. The reaction to the Frei test was positive. Digital examination of the rectum revealed a stricture which did not admit the tip of the index finger. Barium enema showed a stricture involving the rectum and sigmoid. At the time of the colostomy operation the roentgenologic findings were confirmed. The patient was discharged two weeks later, improved.

CASE 5.—*Double stricture of the rectum, rectal fistula, pencil-like stools and blood and pus from rectum on defecation.*

The patient was a white man 35 years of age. There was a history of ulcer of the penis followed by bubo eleven years before admission. During the past eight years he has suffered from constipation. Eight months ago he began to have pencil-like stools and passage of blood and pus from the rectum. Five months ago a rectal fistula developed. Barium enema showed a narrowing annular stricture of the rectum 5 cm. in length. With the patient under spinal anesthesia, one stricture was found  $1\frac{1}{2}$  inches (3.8 cm.) from the anus, and after this was dilated a second stricture was found  $2\frac{1}{2}$  inches (6 cm.) from the anus. These were dilated, and he was discharged, improved.

The foregoing cases are typical of the symptoms and physical findings noted in the majority of cases of rectal stenosis and are highly characteristic.

CASE 6.—*Stricture of the rectum with rectovaginal fistulas.*

The patient was a Negro woman 40 years of age who entered the hospital complaining of passage of stool through the vagina. Seven years ago she began to have many rectal abscesses, and four years ago she began to pass feces through her vagina. She had complained of mucous diarrhea and had lost some weight during the past year. Physical examination showed a fistulous opening into the vagina 1 inch (2.5 cm.) above the fourchet and a stricture of the rectum  $\frac{1}{2}$  inch (1.27 cm.) above the anal orifice, which barely admitted the tip of a finger. Reaction to the Frei test was strongly positive. The Kahn test elicited a negative reaction. While under a regimen of high colonic irrigations, the patient left the hospital one week later, without permission.

CASE 7.—*Stricture of the rectum, with ulcers of the vulva.*

The patient was a Negro woman 48 years of age. She had had three children, the last child now being 24 years of age. The chief complaint was pruritus vulvae, urinary incontinence and painful defecation. The patient had visited many clinics during the past six years, without relief, and the continuous dribbling of urine was particularly disturbing to her. On physical examination she showed the urethral meatus everted, and the external genitalia were deformed by a sloughing off of the posterior extremities of the labia. On separation of the labia, there were several areas of varying size where the mucosa was missing and the submucosal tissue presented. A tight stricture of the rectum was noted on digital examination of the rectum. The Kahn reaction of the blood was negative, and the urine was normal. The blood count showed 3,840,000 red cells, 60 per cent hemoglobin and 7,400 leukocytes, with 62 per cent polymorphonuclears. Under conservative treatment the patient improved, and she left the hospital three weeks later.

CASE 8.—*Stricture of the rectum, elephantiasis of the right labia and sloughing of the rectovaginal septum; colostomy; stricture of the left inguinal colostomy necessitating a second colostomy in the transverse colon.*

The patient was a Negro woman 36 years of age. She entered the hospital complaining of pain on defecation, blood and pus in the stools. Her blood pressure was 140 systolic and 100 diastolic. The patient stated that she had had a recto-vaginal fistula since the birth of a child five years previously. Eighteen months ago she noticed that her stools were becoming smaller and defecation painful and that she had lost 16 pounds (7.3 Kg.) in weight. She had received a course of antisyphilitic treatment. On physical examination there was found an old laceration of the vaginal floor, extending down to the anterior rectal wall. Vaginal examination revealed a tender rectum that was filled with fecal material. On rectal examination a tight stricture  $\frac{1}{2}$  inch (1.27 cm.) above the internal sphincter was found. The Frei test elicited a positive reaction. A left inguinal colostomy operation was performed, at which time many adhesions were found around the sigmoid. Eighteen months later the patient was readmitted to the hospital, owing to cicatrization of her inguinal colostomy to such a point that it was necessary to perform a colostomy in the transverse colon.

The foregoing 3 cases illustrate some of the external manifestations that occur in association with strictures of the rectum in women.

CASE 9.—*Stricture of the rectum ruptured from bougie dilatation; recovery.*

A Negro woman 29 years of age was admitted to the hospital complaining of generalized abdominal pain. On the morning of admission the rectum was dilated by means of bougies in the outpatient department clinic. One-half hour after returning home she was seized with acute abdominal pain and vomiting. Examination showed blood pressure of 92 systolic and 60 diastolic. The abdomen was rigid and tender throughout. On rectal examination blood was found on the examining finger, and there was a stricture admitting the finger, which was tender on pressure. An emergency laparotomy was performed; this operation revealed a perforation of the rectosigmoid. A moderate amount of pus and fecal matter was found in the peritoneal cavity. A 1 inch (2.5 cm.) linear opening in the rectosigmoid was present, and the edges seemed slightly gangrenous. This was repaired by means of continuous silk sutures. Cecostomy was performed through a right gridiron incision, a mushroom catheter being used. The course was uneventful, and the patient was discharged two weeks later.

CASE 10.—*Stricture of the rectum and hemorrhage from instrumental dilation of stricture.*

A Negro woman 26 years of age entered the hospital complaining of bleeding from the rectum. The patient gave a history of constipation and rectal bleeding during the past year. On the day before admission she went to a local physician, who dilated the stricture, and she bled profusely on that day. On admission the patient had a pulse of 130, temperature of 94.4 F and blood pressure 112 systolic and 96 diastolic. On rectal examination she showed moderate bleeding of the rectum, with clots. The anal sphincter was relaxed, and the anal canal was filled with clots of blood. Under conservative treatment she was discharged nine days later, improved.



CASE 11.—*Stricture of the rectum, unsuccessful results with Jelk's operation and perforation of the rectum due to dilation with bougies; death, autopsy.*

The patient was a Negro woman 30 years of age.

*First Admission.*—There was a history of a rectal operation twelve years before admission, while eight years before admission she began to have difficulty in moving her bowels and passed blood at times; this difficulty had increased, and she began to pass pus per rectum and lost several pounds in weight during the past three months. Rectal examination showed thickened mucosa and a stricture  $1\frac{1}{2}$  inches (3.8 cm.) above the anal orifice. Six days after admission an incision was made through the ischiorectal fossa on each side, and by blunt dissection the perirectal exudate was broken up and freed from the rectal wall and the rectal wall was incised. There was also found at operation a second stricture 4 inches (10 cm.) above the anal margin, which would not admit the tip of the finger, and the perirectal exudate around this was broken up and the rectal wall was incised. A posterior proctotomy was also performed, and the patient was discharged fifteen days later, improved.

*Second Admission.*—Two and one-half years after the first admission the patient was readmitted. She had been receiving weekly dilations in a proctology clinic. The day before admission dilation was done with bougies, and severe pain developed in the abdomen and rectum. The pain was cramplike in character and increased in severity. She vomited twice. On admission her temperature was 100 F., pulse rate 100 and respiratory rate 20. The abdomen was slightly distended and exhibited tenderness and rebound tenderness, most pronounced in the left lower quadrant. An emergency laparotomy operation was performed, at which operation a perforation 1 cm. in diameter was found on the antimesenteric border of the sigmoid at a point 2 inches (5 cm.) proximal to the rectosigmoid junction. A thick purulent exudate was scattered over the pelvic organs and covered several loops of bowel. The sigmoid at the point of rupture was soft and was not thickened or indurated. A colostomy was performed through a left McBurney incision above the site of the wound. Culture from the abdomen at the time of operation revealed *Escherichia coli*. The patient died three days later.

*Postmortem Findings.*—Lungs: On section both lungs proved to be extremely congested and hyperemic, and a small amount of thin whitish fluid could be expressed on squeezing.

Abdomen: Located in the pelvis, surrounded by intestine, was a large abscess containing fecal-smelling purulent material. The intestine formed the superior wall of the abscess. The abdominal wall, fascia and parietal peritoneum consisted of a gangrenous slough, which extended from the lower midline incision to the left, involving the whole of the parietal wall, the diaphragm and the lumbar region, down to the pelvis.

Gastrointestinal Tract: Located approximately 8 inches (20 cm.) from the anorectal junction was a 1 inch (2.5 cm.) perforation, three fourths of which was repaired with chromic gut and the other one fourth of which was opened. For an area extending 10 inches (25 cm.) above the anorectal junction, the lumen of the rectum and rectosigmoid was narrow and showed flattening of the rugae. Surrounding the rectum was a large, firm mass, measuring about 10 cm. in diameter, which consisted of lipomatous tissue, with numerous white fibrous strands running through it. Located at the anorectal margin on the mucosal surface of the rectum were numerous fistulous tracts which had blind ends.

*Gross Pathologic Diagnosis.*—The following diagnosis was made: (1) perforation of the rectum, with pelvic abscess and gangrenous slough of the fascia and peritoneum of the anterior abdominal wall, diaphragm and lumbar region, (2) colostomy, (3) rectal stricture (lymphogranuloma inguinale), (4) perihepatitis and perisplenitis and (5) visceral congestion.

*Microscopic Diagnosis.*—The microscopic diagnosis was (1) acute peritonitis, (2) lymphogranuloma, (3) necrosis of the fascia of the abdominal wall, (4) perihepatitis and perisplenitis, (5) pulmonary edema and (6) visceral congestion.

The foregoing case is an example of Jelk's operation with unsuccessful results, because this patient returned two and one-half years later and died from perforation of the stricture.

*CASE 12.—Stricture of the rectosigmoid; death due to peritonitis from a ruptured diverticulum of the sigmoid; autopsy.*

A Negro woman 38 years of age was admitted to the hospital in coma. The history was obtained from her sister, who stated that she had had a rectal stricture for many years and had been receiving treatment for it privately during the past six months. Four days before admission she began to have frequent bowel movements and passage of a small amount of feces through the vagina and complained of abdominal pain and vomiting. Physical examination revealed a moribund Negro woman, who was pulseless and gasping for breath. Her abdomen was distended and tense. A Levine tube was passed, and an infusion of isotonic solution of sodium chloride and a blood transfusion were given at once. The patient died four hours later.

*Postmortem Findings.*—The peritoneal cavity contained about 300 cm. of an admixture of foul greenish brown fecal and purulent material. There were many fine adhesions between portions of the small intestine and the parietal peritoneum in the region of the incisional scar as well as at the cervical stump. Solid dark brown fresh fecal material was seen in the peritoneal cavity in the pouch made between the lower part of the sigmoid colon and the pelvic peritoneum.

*Gastrointestinal Tract:* The stomach and small intestines were grossly normal except for purulent coating. The colon was intact, but in the sigmoid portion in its terminal region were seen several fairly wide diverticula, measuring each approximately 2 by 3 cm. A mass was felt encircling the intestine at approximately the rectosigmoid junction. This mass was about the size of an orange and extended mainly as a posterior collar. On section this mass appeared as a palisaded, fairly firm, yellowish, fatty, fibrinous tissue and was completely encapsulated. In this region the sigmoid and rectum were both somewhat thickened and constricted, barely admitting one finger. Four centimeters above this constriction in the sigmoid, in the left anterolateral length, there was an elongated ragged ulceration, measuring 2.5 cm. in length, and extending from this in the pelvis, retroperitoneally as well as intraperitoneally, there was a large, soft mass of friable tissue, composed mainly of foul, dark brown, old fecal material surrounding the pelvic contents and extending also retroperitoneally in the left flank as far superiorly as the spleen. Anteriorly at the beginning of the anus there was a narrow double sinus tract communicating with the most anterior portion of the vagina.

*Genitalia:* The vagina appeared normal except for the fistulous tract in the extreme anterior portion.

*Gross Pathologic Diagnosis.*—The diagnosis was granuloma venereum with rectosigmoid stricture, rectovaginal fistula, diverticulosis of the sigmoid with rupture and extension, intraperitoneally and retroperitoneally, generalized peritonitis, septic liver, left interligamentous cyst, old parasplenitis with calcification and a healed hilar lesion of tuberculosis.

Cases 9 and 10 are cases showing some of the complications that may result from dilation with bougies in which the patients live. Case 11 proves that such dilations are not without danger. Case 12 is the first case that has been reported of a perforated diverticulum with death as a result of rectal stricture. David and Lauer cited a case of Phemister's in which chronic diverticulitis of the rectum resulted in extreme tubular constriction of the rectum. Phemister resected the rectum and the first part of the sigmoid in a youth, aged 20, who had a history of stenosis of the rectum for seven years. The resected rectum was in the form of a narrow tube. There were several diverticula in the rectum, the largest of which had an opening about 1 cm in diameter into the rectum and penetrated for about the same distance into the thickened rectal wall. Microscopic examination showed the rectal wall to consist of dense fibrous tissue with round cell infiltration.

*CASE 13.—Rectal stricture with thrombophlebitis of the left leg.*

A Negro woman 39 years of age entered the hospital with pain and tenderness of the left leg for the past three days. Her rectum had been dilated in our proctology clinic several times. On examination the left leg was edematous and tender. The temperature, pulse rate and respiratory rate were normal. Blood pressure was 140 systolic and 100 diastolic. The reaction of the blood was negative. On rectal examination she showed a tight stricture, which admitted the tip of the finger. The pain subsided, and the patient left the hospital thirteen days later improved.

(It has seemed rather remarkable to us that so few of these patients showed thrombophlebitis as a complication.)

*CASE 14.—Rectal stricture with hydrarthrosis of left knee joint; diabetes mellitus.*

The patient was a Negro woman 30 years of age.

*Past History.*—She had had inguinal adenitis on the right side ten years before admission. She had constipation and narrow stools for the past two years, with blood in the stool at times, together with loss of weight. Her left knee joint had been swollen and painful for the past two weeks. On physical examination a rectal stricture was found, which barely admitted the tip of the finger. The urine showed glucose (3 plus). Culture from the knee joint was sterile after forty-eight hours. The aspirated fluid was amber colored. The stricture was dilated with the patient under spinal anesthesia. The patient left the hospital one week later, without permission.

*CASE 15.—Stricture of the rectum and descending colon with polyarthritis.*

A Negro man 46 years of age entered the hospital with a history of pain in his joints. During the past three years he had diarrhea and bloody stools and lost 15 pounds (6.8 Kg.) in weight. On abdominal examination a mass the size of an

orange was felt to the left of the umbilicus, which was tender; the abdomen was soft, and ankles, wrists and elbows were swollen, hot and tender. Four days after admission he showed gross blood in his stools. Sigmoidostomy showed several small ulcerations of the rectum and 7 inches (17.7 cm.) above the rectum there was a stricture. The Frei test elicited a positive reaction. The Kahn test gave a 1 plus reaction. A barium enema showed pronounced diffuse narrowing of the descending colon and sigmoid and part of the rectum. The total protein content was 5.12 mg. per hundred cubic centimeters, albumin 2.69 mg., globulin 2.43 mg. and albumin-globulin ratio 1.2 mg. The patient left the hospital after receiving sulfonamide drugs, one week later, improved.

CASE 16.—*Stricture of the rectum with arthritis of the right hip joint.*

The patient was a Negro woman 42 years of age. Three years before admission the patient had an impassable stricture of the rectum. Her chief complaint was pain in the right hip joint and swelling of the right thigh, which had grown progressively worse. Examination showed a permanent artificial anus in the left lower quadrant. Rectal examination revealed an impassable stricture of the rectum. The right leg was swollen, tender and darker than the left. A roentgenogram showed a narrowing of the joint space of the right hip joint. The Frei test gave a strongly positive reaction. The patient remained in the hospital for one week and eventually remained under observation for three years, still complaining of her hip joint.

Cases 14, 15 and 16 are examples of arthritis of varying types which have occurred in this series of cases. Arthritis is not an uncommon manifestation of lymphogranuloma venereum.

CASE 17.—*Stricture of the rectum associated with bone changes.*

A Negro man 46 years of age had received rectal dilations and injections of Frei antigen in the clinic for many years. He had been to many hospitals, complaining of constipation and abdominal pain. On admission his temperature was 100 F., pulse rate 98 and respiratory rate 24. The patient showed a stricture of the rectum 2 inches (5 cm.) above the anus, obstructing the lumen. A biopsy specimen was taken from the stricture, and the pathologic report was lymphogranuloma venereum. Colostomy was done. Roentgenograms that were made of the spine and pelvis showed areas of rarefaction of the lumbar portion of the spine as well as of the pelvis. The patient had been admitted to the hospital three times, and he came into the hospital three years later with pneumonia of the lower lobe of the right lung, from which he died. Unfortunately, no autopsy was obtained.

The preceding case is one of osseous changes associated with lymphogranuloma venereum, which is relatively infrequent (figs. 11 A and B).

CASE 18.—*Rectal stricture, partial intestinal obstruction; no operation; recovery.*

A Negro woman 45 years of age entered the hospital with a history of vomiting for the past three weeks. Five years before she had a swelling of inguinal glands on the left side. Two years ago she noticed extreme constipation. She has had a poor appetite and has lost a considerable amount of weight during the past year, during which time her stools have been ribbon-like and occasionally blood streaked. Three months before admission constipation became severer, and she had colicky, epigastric pains. When examined the patient was a pale, emaciated, dehydrated

woman, with a distended tender abdomen. A rectal stricture was found, which did not admit the tip of the finger. The temperature, pulse rate and respiratory rate were normal. The blood cell count showed 3,980,000 red cells and 8,800 white cells, with a hemoglobin content of 70 per cent. The blood pressure was 150 systolic and 102 diastolic. She gave a positive reaction to the Frei test and a 3 plus reaction to the Wassermann test. Examination of the urine gave essentially normal results. A roentgenogram of her abdomen revealed distended loops of large and small bowels but no fluid levels. A barium enema showed a definite narrowing of the rectum, extending up to the lower part of the sigmoid, and above this point the sigmoid was distended. The patient was treated with high colonic irrigations and finger dilations, and she left the hospital ten days later, improved.

CASE 19.—*Rectal stricture with acute intestinal obstruction; colostomy; recovery.*

A Negro woman 31 years of age entered the hospital complaining of abdominal pain and vomiting. She had had abdominal pain for the past nine days, which at times was cramplike in character and at other times a constant distressing ache. The abdomen was distended and tender throughout. On vaginal examination the uterus was found to be retroflexed, and there was tenderness in both fornices. Digital examination of the rectum revealed a tight, impassable annular stricture  $1\frac{1}{2}$  inches (3.8 cm.) above the anus, with hard nodular edges. Conservative treatment was followed for three days, at the end of which time her vomiting continued and roentgenologic examination of the abdomen showed considerable gas in the large and small intestines, with fluid levels. Her reaction to the Kahn test was 4 plus. Colostomy was performed as an emergency measure. She left the hospital twenty days later, without permission.

CASE 20.—*Rectal stricture with acute intestinal obstruction; death; autopsy.*

A 70 year old Negro woman was admitted to the hospital, acutely ill and dehydrated. Her past history was that thirty-five years previously she had been operated on for a stricture of the rectum and that since that time she had been incontinent of feces. Four years after the first operation she was unsuccessfully operated on again to control her incontinence. Her present illness began the day before admission, at which time periumbilical pain developed and she vomited several times. Physical examination on admission revealed: The tongue was dry, the mucous membranes pale and the abdomen distended; there was no visible peristalsis and no palpable masses; the liver was not enlarged, and there was no rigidity or spasm of the abdominal muscles. The blood pressure was 140 systolic and 90 diastolic. Rectal examination showed a definite stricture 2 inches (5 cm.) above the anus, which did not admit the tip of the index finger. The temperature was 101.8 F., pulse rate 108 and respiratory rate 36. The red blood cell count was 3,700,000 and the white blood cell count 45,000, with 89 per cent polymorphonuclears. The hemoglobin was 70 per cent. A flat roentgenogram of the abdomen revealed distended loops of large and small bowels with fluid levels. Operation was advised, but it was refused by the patient. The patient was given supportive treatment, but she died ten hours after admission.

*Postmortem Findings.*—There was no consolidation of the lungs, although they were reddish purple and moderately anthracotic. The trachea and bronchi contained moderate amounts of frothy serosanguineous fluid. The tracheal and bronchial mucosa was diffusely congested. The heart was flabby and large and weighed 380 Gm. The aorta showed several irregular atheromatous plaques. The

colon and ileum were distended with gas and fluid. The wall of the rectum, about 8 cm. below the sigmoid flexure, felt indurated and somewhat pipe stemmed. No free fluid was present in the peritoneal cavity. The hepatic flexure of the colon was adherent to the gallbladder, and several bands of adhesions connected the first portion of the duodenum to the gallbladder. The rectum was strictured and admitted only the little finger. When the lumen was opened, the stricture was noted to extend for a distance of 16 cm. The mucosal folds were lost, and the mucosal surface appeared smooth, gray and fibrosed, almost hyalinized. Five centimeters above the anal rectal junction was an ulcerated area 1 by 0.5 cm. The ulceration was superficial, the edges were irregular and a small bony concretion was lodged in the floor of the ulcer at its lower pole. No hemorrhoids were present. The wall of the stricture felt moderately firm and indurated. On section a fairly smooth, gray, fibrotic surface was noted. Proximal to the stricture, the colon and practically the entire ileum appeared moderately distended with gas and dark brown fecal fluid. The serosal surfaces were grayish brown, and the serosal vessels were moderately injected. The distentions of the intestine diminished from the ileum to the jejunum, and in the latter segment of the bowel no distention was present. The mucosa of the distended intestine was fairly smooth and the villous folds almost completely absent. The stomach and duodenum were not unusual. No ulcerations of the small intestine were present.

*Pathologic Diagnosis.*—The diagnosis was acute intestinal obstruction due to rectal stricture caused by lymphogranuloma venereum, edema of the lungs, atherosclerosis of the coronary arteries and thoracic aorta, hypertrophy of the left ventricle, fibrosis of the mitral valve, cloudy swelling of the heart, liver and kidneys, diaphragmatic-hepatic adhesions, diaphragmatic-splenic adhesions, perisplenitis, arteriolosclerotic kidneys, atrophic ovaries and atrophy of the uterus, tubes and ovaries.

*CASE 21.*—*Rectal stricture with acute intestinal obstruction due to volvulus of the ileum; congenital elongated mesentery; postoperative pneumonia; death; autopsy.*

A Negro woman 59 years of age entered the hospital complaining of abdominal pain and vomiting. She had been constipated for many years, and, ten years before, she had had an operation for hemorrhoids. During the past months she had lost her appetite, lost weight and felt weak. Five days before admission, a pain developed in the epigastrium and she began to vomit. The next day she had a bowel movement, but there had been none since. On physical examination the patient was found to be an emaciated, acutely ill woman. On rectal examination an annular constricting mass which began 2 inches (5 cm.) above the anal verge and extended upward was found, but its upper limit could not be felt. The mass formed a stricture, which admitted only the little finger. The clinical diagnosis was acute intestinal obstruction due to stricture of the rectum. On the day of admission a duodenal tube was passed, and 2,000 cc. of fecal material gushed out. An infusion of isotonic solution of sodium chloride was given. A roentgenogram of the abdomen showed the small intestines distended with gas and the presence of fluid levels. An emergency laparotomy was performed, and at operation a loop of ileum several feet in length was found tucked under a segment of the mesentery. The portion of intestine proximal to the volvulus was distended, and the intestine below was collapsed. The volvulus was reduced and the abdomen

closed. The patient's temperature on admission was 100 F., and after the operation it rose to 104.6 F. and fell to 99 F.; it rose again to 104 F. just before death.

*Laboratory Data on Admission.*—The blood chloride level was 370. The Kahn reaction of the blood was negative. The white blood cell count was 28,000, with polymorphonuclears 89 per cent, and the red blood cell count was 5,100,000. The patient died seven days after operation. Death was due to terminal lobar pneumonia of the lower lobe of the right lung and edema of the middle lobe of the right lung and lower lobe of the left lung.

*Autopsy Findings.*—The serosal surface of the third portion of the duodenum, the jejunum and the proximal half of the ileum were grayish blue and gray, and the vessels were moderately injected. The mucosal surfaces were decidedly injected. The valvulae conniventes appeared edematous and congested. The mucosal surfaces of the colon were not flattened. When the rectum was opened, the mucosa showed several small superficial ulcerated areas extending from the anorectal junction proximalward for a distance of 6 cm. The mucosa was brownish gray, and the wall was moderately thickened and indurated. A few of the perirectal nodes were enlarged, pea sized and moderately firm. On section they had a homogeneous, pale gray, granular appearance. The final pathologic diagnosis was terminal lobar pneumonia of the lower lobe of the right lung, edema of the middle lobe of the right lung and lower lobe of the left lung, acute enteritis involving the third portion of the duodenum, jejunum and proximal half of ileum, congenitally elongated mesentery, rectal stricture, pronounced congestion and cloudy swelling of the kidneys (arteriosclerotic), cloudy swelling and fatty parenchymatous degeneration of the liver, atherosclerosis of the coronary arteries and thoracic aorta, multiple superficial ulceration of the esophagus (Levine tube) and decubitus ulcers of the sacral region and buttocks.

The foregoing 4 cases of intestinal obstruction of varying degree are typical of the commonest complication of rectal strictures. It is of interest to note that the most frequent and serious obstruction is in persons over 40 years.

• *CASE 22.—Rectal stricture simulating ulcerative colitis.*

The patient was a Negro woman 28 years of age.

*First Admission.*—She entered the hospital with a history of frequent stools that numbered eight to twelve a day, containing blood and mucus, and pain in the left lower quadrant when she had a bowel movement. On physical examination a slight tenderness was noted in lower part of the abdomen. Inspection showed external hemorrhoids. Rectal examination showed a slight stricture with a granular, red mucosa. Sigmoidoscopic examination revealed acute and chronic ulceration as far as the sigmoidoscope would reach. The flat roentgenogram of the abdomen was normal. The Kahn reaction of the blood was negative. Cultures of the blood were sterile. No ova or parasites were found in the stool.

*Second Admission* (six months later).—The patient complained of vomiting, abdominal distention with attacks of diarrhea, chills and fever. A roentgenogram of the chest was normal. Repeated examination of the sputum was negative for tubercle bacilli. Examination of the rectum showed a well developed stricture, which barely admitted a tip of the index finger, with chronic ulceration above the strictured area. Colostomy was advised, but it was refused by the patient, who went home without permission.

CASE 23.—*Stricture of the rectum; colostomy followed by intrasphincteric amputation of the rectum (Pauchet's method).*

A Negro woman 38 years of age entered the hospital complaining of constipation, pain on defecation and discharge of pus through the rectum. She had had occasional vomiting and dizzy spells. Four years before admission she had been operated on for fistulas in ano. The blood pressure was 100 systolic and 72 diastolic. The red blood cell count was 1,500,000, the white blood cell count 7,800 and the hemoglobin content 76 per cent. The Wassermann test gave a 4 plus reaction. Studies of blood chemistry showed creatinine 1.1 mg., urea nitrogen 14.4 mg. and sugar 78 mg. per hundred cubic centimeters. Temporary colostomy was performed. One month later the rectum was resected and the stricture excised, the sphincter being preserved according to Pauchet's technic, after which she was allowed to go home. Three months later she returned, and the spur was crushed and the colostomy closed. One month later she was discharged home, well.

Twenty-six cases in which this operation was used were reported by us in another article.<sup>1e</sup>

CASE 24.—*Stricture of the rectum and perforation of the rectum from rectal irrigation; death; autopsy.*

The patient was a Negro woman 25 years of age. The day before admission she had been struck over the head, following which she lost consciousness but quickly recovered. On admission the patient showed a hematoma of the forehead and left eye. Her past history was that she had had a fistula in ano since she was 13 years of age. Four years before, the patient was operated on for a pelvic condition, and since that time she had had pain on defecation and discharge from an anal fistula. The reaction to the Frei test was strongly positive. Rectal examination showed a scar above the anus resulting from a previous operation and a fistula to the left of the anus. A stricture was present  $\frac{1}{2}$  inch (1.2 cm.) from the anal verge, which admitted a finger. She was being treated in the hospital with rectal irrigation. Seventeen days after admission, after one of her rectal irrigations, she complained of severe abdominal pain and vomited three or four times. At that time the surgeon felt that there was a possibility of a perforation of one of the granulomatous areas following the irrigation. Two days later the abdomen was distended, tender and rigid, but she stated that similar episodes had happened before. A week later the diagnosis was peritonitis and pelvic infection, and the surgeon felt that the peritonitis was localizing and nonoperative. The patient died ten days later.

*Autopsy Findings.*—The abdomen was distended. The omentum was plastered down into the pelvis and over the small and large intestine. The loops of intestine were matted together by fibrous adhesions, which were fairly firm. In both abdominal troughs there was present a thick, creamy pus. This pus was also present under the diaphragm on the right side. The anterior surface of the right lobe of the liver was covered with a layer of fibrin and pus.

Gastrointestinal Tract: The mucosa of the small intestine was friable; however, no ulcerations could be made out, the friability being due to the peritonitis and pus in the wall of the blood vessels themselves, the pus due also to peritonitis. The large intestine was normal in appearance. At a point about 8 inches (20 cm.) from the rectum the mucosa of the rectum and sigmoid became thickened and had a grayish color. The mucosa lay in folds in places and looked like



the tentacles on a squid. Multiple strands of fibrous tissue ran through the mucosa, the entire wall was thickened and narrowed and the lumen was constricted. Near the rectum there were two large ulcerations, each about  $\frac{1}{2}$  inch (1.2 cm.) in diameter. The bases of the ulcers were necrotic, and in the centers of the ulcers were small openings, which were  $\frac{1}{4}$  inch (0.6 cm.) in diameter, which opened into the tissue in back of the rectum.

**Reproductive Organs:** The rectovaginal wall was thickened and infiltrated. Both tubes were distended and contained pus. The left ovary was normal, and the right ovary could not be located.

**Spleen:** The spleen was enlarged to about three times its normal size and was septic in appearance.

**Anatomic Diagnosis.**—The diagnosis was lymphogranuloma inguinale, stricture of the rectum, ulcerative proctitis, congestion and edema of the lungs, ecchymosis of the left eyelids and fistula of the rectum.

**Cause of Death.**—The cause of death was lymphogranuloma inguinale, stricture and ulcer of the rectum and acute suppurative peritonitis.

**CASE 25.**—*Rectal stricture, rectovaginal fistulas, anal fistulas, duodenal ulcers, esophageal varices; colostomy; death from pneumonia.*

The patient was a Negro woman 49 years of age.

**First Admission.**—She entered the hospital complaining of abdominal pain. She gave a history of having had a colostomy performed in a hospital in Connecticut for what she was told was a growth in the rectum, before which time she had extreme constipation. Her reaction to the Frei test was positive. On admission she complained of abdominal pain and, in spite of her colostomy, a discharge of her fecal material through the vagina when she had a bowel movement through the rectum, which was two or three times a day. She was advised to have a colostomy in the transverse colon but refused.

**Second Admission.**—One year later she was admitted to the medical service because of pain in the right side of the chest, cough and chills. Six weeks prior to admission she had been in bed because of generalized weakness. Her blood pressure was 78 systolic and 60 diastolic, the pulse rate was 120 and the respiratory rate 28. There was tenderness over the lower lobe of the right lung and impaired resonance posteriorly. Roentgenograms showed pneumonia of the right middle and lower lobes of the right lung. Type III pneumococci were obtained from the sputum. The patient was treated with sulfadiazine and died three days later.

**Autopsy Findings.**—There was present a colostomy in the left lower quadrant, which barely admitted the tip of a small finger.

**Lungs:** The entire right lung was completely consolidated, hard and dull gray, except for the apical tip. The cut surface revealed a uniform grayish consolidated appearance, with a purulent discharge exuding from the bronchi.

**Abdomen:** The lower end of the esophagus contained three or four dilated varices, one of which was thrombosed. The first part of the duodenum contained an elliptic-shaped ulcer about 1 cm. in diameter, with a ragged edge and a granular base. The surrounding area was somewhat indurated, and there were four smaller ulcerated areas in the vicinity about 2 mm. in diameter, with the edges thickened and indurated. The rectum was dark red and congested but not stenosed or stricture. However, the perirectal tissues were decidedly indurated and thickened,

and the anal canal contained numerous fistulous tracts opening up into the external anal area. The mucous membrane of the rectum and the anal canal was hemorrhagic.

Liver: The liver was enlarged, and the right lobe contained a fibrinous exudate over the capsule.

The gross pathologic diagnosis was lobar pneumonia of the lower, middle and upper lobes of the right lung, confluent bronchopneumonia of the lower lobe of the left lung, varices of the esophagus, multiple chronic duodenal ulcers, lymphopathic disease of the rectum with a waterpot anal fistula and old sigmoid colostomy.

(This case illustrates the debilitating effects of a rectal stricture, which undoubtedly was the major predisposing cause of her fatal pneumonia.)

CASE 26.—*Stricture of the rectum, perineal resection of the rectum; recovery.*

The patient was a Negro woman 26 years of age, who had a colostomy for a rectal stricture three months before she was admitted to the hospital. Multiple scars were present over the buttocks from abscesses resulting from the stricture. Perineal resection of the rectum was done, and all diseased tissue was excised. The rectum was found strictured throughout its extraperitoneal length. The healthy rectal mucosa was sutured to the skin, with the sphincter preserved. Pathologic examination of the excised rectum gave the following diagnosis: lymphogranuloma venereum of the rectum, showing giant cells, plasma cells and focal and round cell infiltration. The patient was discharged from the hospital one month later.

CASE 27.—*Stricture of the rectum, urethral stricture.*

The patient was a Negro man 46 years of age. For the past year he received treatment for urethral strictures; at the same time he noticed severe constipation, pain on defecation and a purulent discharge from the perianal area. A urethral stricture was found to be present, which with difficulty admitted a size 20 French sound. Several pinpoint openings were present in the perineum, and from each opening there was a discharge of purulent material. One inch (2.5 cm.) above the sphincter there was a stricture, which admitted only the tip of the examining finger. The patient remained in the hospital five days and left without permission.

#### SUMMARY

Strictures of the rectum due to lymphogranuloma venereum are a serious threat to life in some instances. Negro women are chiefly affected. Some conditions are mild and seem to cure themselves. Other conditions progress in spite of all known methods of treatment. It is our opinion that these variations in clinical behavior result from the fact that there are different strains of the virus and that the virus produces a reaction according to the host. The early diagnosis and treatment in all cases is important. In the prestricture stage sulfonamide compounds seem to have some value, but there is a question as to whether sulfonamide drugs can prevent permanently an extension of the processes in some cases. It is likewise true that in some of the instances in which sulfonamide drugs seem to have been of value the evidence is not conclusive as yet that these patients might not have done as well without the sulfonamide compounds as far as checking the activity of the virus is concerned. Sulfonamide drugs do help in clearing up the

secondary superimposed infections that are present in these cases and thus improve the condition of the patient clinically. Penicillin has proved valueless in our hands. Once a fibrous stricture has occurred, drugs are of value only by elimination of the toxic effect of secondary bacterial invasion due to the fact that the blood supply to and through the dense scar tissue is so lessened that no adequate therapeutic concentration of the drug is possible.

Some conditions do not progress rapidly and are not serious, while other conditions do progress rapidly in spite of all forms of treatments, with the exception of early excision. Colostomy helps many patients (1) by lessening secondary infection and (2) by overcoming the toxic effects of chronic obstruction of the bowel. Surgical treatment alone is of value once a fibrous stricture of any considerable extent is developed. Warthen's obliteration of the cul-de-sac operation offers the possibility of lessening the complications that are inherent in colostomies, namely, anterior grade and retrograde herniation. It cannot, however, prevent stenosis of the colostomy opening, which occurs in many instances. Pauchet's excision operation or a modification thereof at this time offers the best method of cure for strictures low in the rectum. This does not exclude the sacroperineal excision operation of Hartmann. These operations are of such magnitude that they should be performed only by experienced surgeons. When the disease involves the entire rectum or is high in the rectum, involving the rectosigmoid area, abdominoperineal extirpation is indicated if the patient's clinical condition does not improve after colostomy. In the rare cases in which the descending colon is involved, a permanent artificial anus in the transverse colon should be made. Carcinoma occurs as a superimposed factor in a sufficiently large number of cases to be of clinical significance.

Much further study is needed to complete our knowledge and understanding of this subject.

## APPENDICITIS

A Review of Nine Hundred and Thirty-Six Cases at the Cincinnati General Hospital

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AND

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IN TWO previous reports from this clinic, all cases of patients with appendicitis admitted to the Cincinnati General Hospital between 1915 and 1934<sup>1</sup> and 1934 and 1939<sup>2</sup> respectively were reviewed. The present study is a continuation of this series and will include all cases of patients with appendicitis treated between Jan. 1, 1939 and Jan. 1, 1944.

In the preceding articles the general trend toward a reduced mortality rate from appendicitis as seen in this hospital was noted. This favorable trend was attributed to (1) the adoption of the McBurney incision in 1922 for appendectomy and (2) the intensive educational campaign concerning management of appendicitis directed toward physicians and the public. This campaign, fostered by the Public Health Federation and the Academy of Medicine of Cincinnati, is still in progress. The sustained and commendable improvement resulting from the campaign may be gaged by a comparison of certain phases of the morbidity and mortality statistics of the present review with those in the preceding articles in this series.

An attempt will be made in this paper to consider certain aspects of the syndrome and treatment of appendicitis in a manner comparable to that employed in the earlier studies. It is not the purpose to uncover new facts concerning appendicitis or its treatment. In bringing to date a study of all cases of patients with appendicitis treated in a large clinic for twenty-nine years, we are advancing toward the objective which was selected when this series of papers was begun. It is our belief that this article and those which precede and will succeed it may serve as references of some value in the presentation of a reasonable, comprehensive concept not only of the general trends in the management of appendicitis but of the various aspects of the disease itself.

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From the Department of Surgery, University of Cincinnati College of Medicine and the Cincinnati General Hospital.

1. Reid, M. R.; Poer, D. H., and Merrell, P.: A Statistical Study of 2,921 Cases of Appendicitis, *J. A. M. A.* **106**:665 (Feb. 29) 1936.

2. Reid, M. R., and Montanus, W. P.: Appendicitis: An Analysis of 1,153 Cases at the Cincinnati General Hospital, *J. A. M. A.* **114**:1307 (April 6) 1940

## PATHOLOGIC CLASSIFICATION

The classification of appendicitis based on clinical and pathologic findings is in accordance with that outlined in the previous papers of the series.<sup>3</sup> The 936 cases in this report were grouped as follows: 605, or 64.6 per cent, were classified as acute appendicitis without perforation; 260, or 27.7 per cent, as acute appendicitis with perforation, and 71, or 7.6 per cent, as chronic or interval appendicitis. Of the 260 cases of acute appendicitis with perforation, 167, or 17.8 per cent

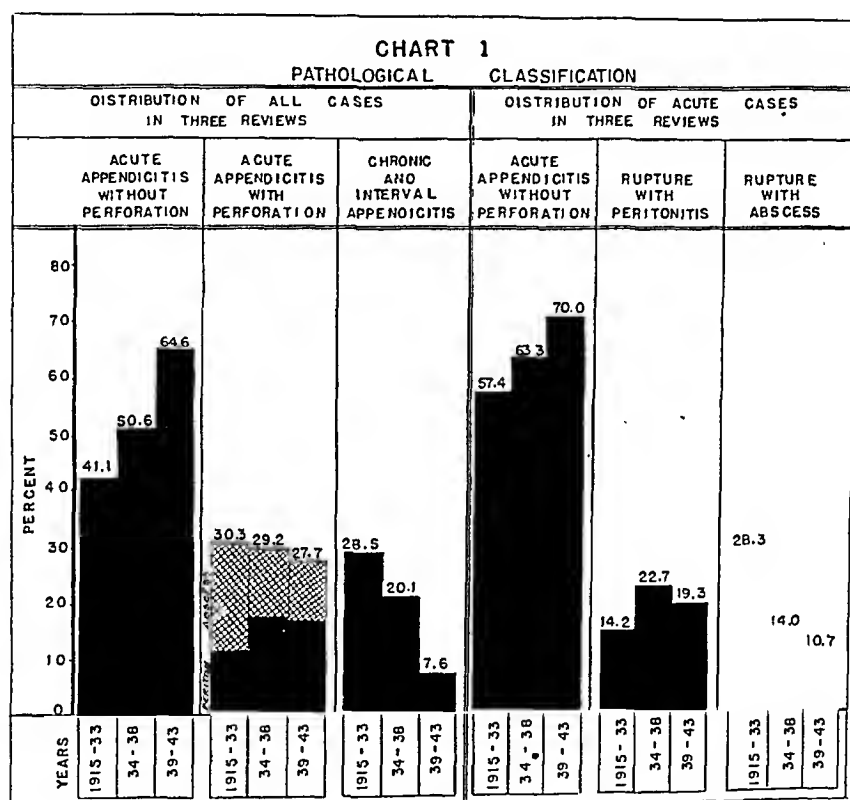


Chart 1.—Pathologic classification of cases of appendicitis.

of the entire series, were classified as acute appendicitis with perforation and generalized peritonitis. The remaining 93, or 9.9 per cent, were classified as acute appendicitis with perforation and abscess. The preceding data, with corresponding statistics for the earlier studies, is presented in chart 1.

The pronounced reduction in the total number of cases (936) as compared with 1,153 cases in the preceding five year period<sup>2</sup> is explained by the decreased census of charity hospitals since 1941. For example, 1,789 major operations were performed in this institution

3. Reid, Poer and Merrell.<sup>1</sup> Reid and Montanus.<sup>2</sup>

in 1943, as compared with 2,232 in 1939.<sup>4</sup> A similar observation was made by Hathaway<sup>5</sup> in 1943.

It may be noted that the incidence of chronic and interval appendicitis in this study is at pronounced variance with that of the preceding reviews. The discrepancy is explained by the elimination in the present series of (1) all cases in which a diagnosis of mesenteric adenitis was made at operation, (2) all cases in which signs and symptoms attributed to chronic or interval appendicitis were not relieved by operation and (3) all cases in which the diagnosis of chronic or interval appendicitis was not substantiated by microscopic examination of the appendix. It would be fitting to reflect that the reduced number of cases of chronic and interval appendicitis in this series results in a corresponding relative increase in the percentage of perforations. A more accurate interpretation may be obtained by the comparison of the proportion of perforations among patients with acute appendicitis, referred to in chart 1.

#### AGE

The average age of all patients in this series was 25.9 years. The decade of highest incidence was that in the years between 11 and 20 (355 cases), while the decade of next highest incidence was that in the years between 21 and 30 (241 cases). Perforation of the appendix followed a similar distribution, 74 and 42 cases in the second and third decades respectively. These observations are in accord with the preceding articles in this series and with recent reviews from other clinics.<sup>6</sup>

It would seem unnecessary to repeat that appendicitis is primarily a disease of youth and that in 107 of the 260 cases of perforation in this series the patients were under 21 years. A rather startling finding in this study, however, was the occurrence of 83 perforations, an incidence of 58 per cent, in the 142 cases of acute appendicitis in patients over 40 years, a finding explained in part by the knowledge that appendicitis in the more advanced age groups may present an atypical syndrome or problems in differential diagnosis not encountered in younger patients. It was interesting to note that the departure of large numbers of young men to the armed forces was not a factor in the decreased census. It was found that the relative incidence of appendicitis among patients in the second or third decades of life varied less than 5 per cent during any of the five years reviewed.

4. Annual Report of the City Manager, Cincinnati, Ohio, 1943.

5. Hathaway, H. R., and Watkins, R. M.: *Economic State and Mortality in Appendicitis*, Ohio State M. J. **39**:247 (March) 1943.

6. (a) Jennings, J. E.; Burger, H. H., and Jacobi, M.: *Acute Appendicitis: A Clinical and Pathological Study of 1,680 Cases*, Arch. Surg. **44**:896 (May) 1942. (b) Busch, I., and Spivack, A. H.: *Observations on Acute Appendicitis: A Series of 635 Cases*, Surg., Gynec. & Obst. **70**:241 (Feb.) 1940.

## SEX

In the present study the well known preponderance of appendicitis in the male is again demonstrated. Of the total of 936 cases, 619, or 66.1 per cent, were in males and 317, or 33.9 per cent, in females. The incidence of perforation in acute appendicitis was 196, or 31.6 per cent, in males, and 64, or 20.1 per cent, in females.

## SEASON

Unlike the preceding review, in which there was an increase of appendicitis in the summer, the greatest seasonal incidence in this series was during the winter months. Two hundred and seventy-three of the 936 patients were admitted during the first three months of the year.

## RACE

The race distribution paralleled that of the hospital census. Six hundred and ninety-two, or 73.9 per cent, of the patients were white, while the remaining 244, or 26 per cent, were Negroes. The incidence of perforation among patients with acute appendicitis in the present series was 173, or 27.2 per cent, among white patients and 87, or 38.2 per cent, among Negroes.

## DELAY IN HOSPITALIZATION

In the previous reviews from this clinic emphasis was placed on the danger attending delay in the seeking of hospitalization for acute appendicitis. It is believed that the campaign to educate the public regarding the syndrome of acute appendicitis has resulted in progressive reduction of the average period between onset of symptoms and hospitalization. We are pleased to report that there has been an additional decrease. The average period between onset of symptoms and hospitalization in the group of patients with acute unruptured appendicitis was 26.6 hours as compared with the mean of 33.1 hours recorded for the preceding five years. In the group classified as acute appendicitis with perforation and generalized peritonitis, the average time elapsing between onset of symptoms and admission was 54.3 hours (64.9 hours in the 1934-1938 series). In patients with perforation and abscess formation, the average elapsed time was 116.5 hours, against 145.9 hours in the 1934-1938 review.

The mean delay in hospitalization for all patients with acute appendicitis was 41.7 hours (chart 3). The figure compares favorably with the average delay in hospitalization (thirty-seven hours) reported by Hathaway and Watkins<sup>5</sup> in their series, since 76 per cent of their patients were admitted to private hospitals. These authors observed that in 1940 and 1941 "staff patients" sought attention on an average of nine hours later than private patients.

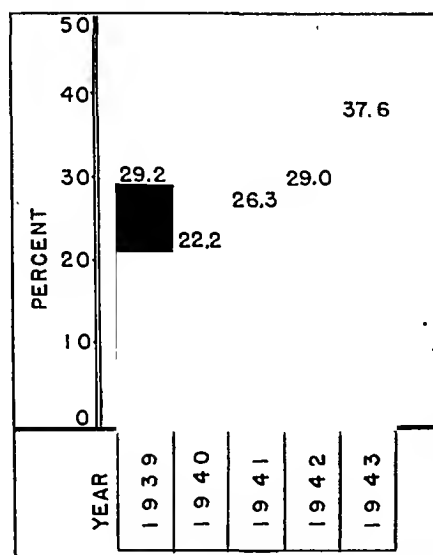


Chart 2.—Incidence of perforation among all cases of appendicitis at the Cincinnati General Hospital in the period 1939-1943.

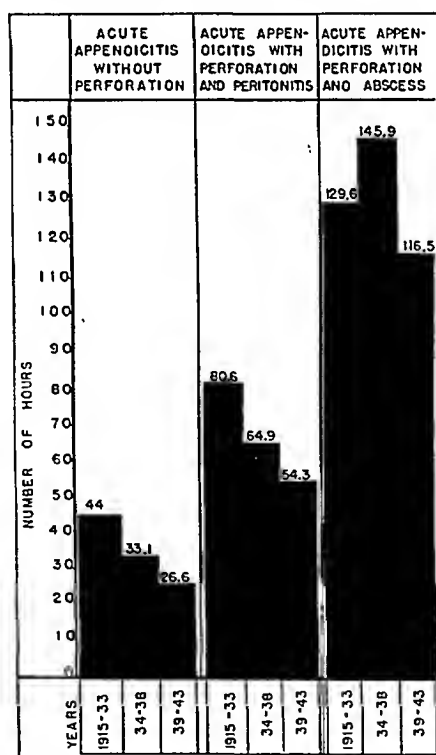


Chart 3.—Time in hours between onset of symptoms and hospitalization.



It is probably worthy of note to compare the elapsed time between onset of symptoms and admission among white patients and Negroes. In all groups, Negro patients were admitted to the hospital at a significantly later hour than white patients (table 5). The relation between elapsed time between onset and admission and mortality rate will be discussed in subsequent paragraphs.

#### CATHARTICS

The earlier articles from this clinic stressed the deplorable use of laxatives prior to hospital admission and described the campaign of education by which the public was informed of the dangers of self medication for abdominal complaints. It is gratifying to find that there has been improvement as regards this phase of the study. Whereas in the 1934-1938 series of 921 patients with acute appendicitis "410, or 44.5 per cent, gave a history of having taken some cathartic,"<sup>2</sup> in this series of 865 cases of acute appendicitis, 329, or 38 per cent, of the patients were known to have taken such medication. This is a decrease of 6.5 per cent. The correlation between catharsis and perforation stressed in this clinic and by others<sup>7</sup> is again shown on examination of the totals. Of 605 cases of acute appendicitis without perforation, in 189, or 31.3 per cent, the patients had taken laxatives, as compared with 140, or 53.8 per cent, of the 260 cases of acute appendicitis with perforation in which there was a history of catharsis.

An interesting aspect of catharsis is found in a comparison of the use of medication by the Negro and white races. Of 141 Negroes with acute appendicitis without perforation, 64, or 45.4 per cent, took laxatives, as compared with 135, or 27.2 per cent, of the 464 white patients with similar condition. The difference was less pronounced among cases of acute appendicitis with perforation, the figures for the respective races being Negro 58.3 per cent and white 51.4 per cent. The most commonly used preparations were magnesium sulfate (102 cases) and castor oil (52 cases). The Negro patients used these two preparations almost twice as frequently as did white patients, 31.2 per cent using them against 16.8 per cent of all patients suffering with acute appendicitis respectively. Among 8 cases in which cathartics were known to have been prescribed by physicians, there were 6 perforations, of which 1 was fatal.

#### CLINICAL DATA

The various physical findings and symptoms occurred with much the same frequency as noted in the preceding reviews. Thus in 865

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7. (a) Reynolds, J. T.: Symposium on Abdominal Surgery. Appendicitis: Basic Considerations in Choice of Therapy, *S. Clin. North America* 24:128 (Feb.) 1944. (b) Footnote 6.

cases of acute appendicitis abdominal pain occurred in 861, or 99.5 per cent, nausea was noted in 363, or 41.9 per cent, and emesis occurred in 581, or 67.1 per cent, while rectal tenderness was noted by the physician in 534, or 61.4 per cent.

If one assumes that the syndrome of acute appendicitis is frequently characterized by pain, nausea, emesis and rectal tenderness, it could be stated that any patient in whom were noted at least three of these signs and symptoms presented the classic picture of appendicitis. It should be pointed out that only 536, or 61.9 per cent of the 865 cases of acute appendicitis may be said to have presented such characteristic clinical pictures.

#### LABORATORY DATA

The mean temperature of all patients with acute appendicitis was 99.9 F. Of the patients with acute appendicitis without perforation the average temperature was 99.5 F., while in the group of patients with acute appendicitis with perforation the mean temperature was 100.8 F. The average white blood cell count in all cases of acute appendicitis was 15,800, whereas in the groups of cases classed as acute appendicitis without rupture and acute appendicitis with rupture the mean white blood cell counts were 15,100 and 17,400 respectively.

#### ANESTHESIA

Anesthesia for appendectomy was again chiefly of the inhalation type. At the time of the last review from this clinic it was "our policy to use nitrous oxide-ether anesthesia when operating on patients with appendicitis."<sup>2</sup> Since the last report, cyclopropane has been used with increasing frequency; thus in 1943 that agent was used for 48.2 per cent of all patients with appendicitis receiving inhalation anesthesia. Spinal anesthesia, used in 13 per cent of all cases, was given formerly in cases "in which general anesthesia was contraindicated."<sup>2</sup> Recently, however, spinal anesthesia has been used for an appreciable number of patients who formerly would have received inhalation anesthesia. Local anesthesia alone or supplemented with other agents was used in a small number of "poor risk" patients (10 cases in all).

#### INCISIONS

In this clinic the McBurney incision is the customary approach to the appendix for reasons which were presented in the initial paper<sup>1</sup> and which are worth repetition: ". . . acute appendicitis can be adequately treated through the McBurney approach, whether it is an unruptured appendix, an appendiceal abscess or peritonitis. Operations so performed are less severe, and postoperative complications such as obstruction, broken-down wounds and ventral hernias are less common. Adequate drainage is more easily and safely secured through a McBurney

incision." In the cases in which there is a question of differential diagnosis between appendicitis and another condition, as cholecystitis, pancreatitis, Meckel's diverticulitis or a twisted ovarian cyst, a McBurney incision is made deliberately, in the belief that no harm will be done should an additional incision be necessary for the management of any other condition. In the cases of questionable diagnosis, the abdomen is draped so that a supplementary laparotomy incision can be made without confusion. In spite of the excellent results with the right rectus incision, reported by Ladd and Gross<sup>8</sup> and Busch and Spivak,<sup>6b</sup> Jennings and colleagues<sup>6a</sup> and Brett and Watkins<sup>9</sup> reported equally convincing results with the McBurney incision.

In the 923 patients on whom operation was performed, the McBurney incision was employed 899 times, the right rectus approach 18 times, a cul-de-sac drainage of a pelvic abscess twice and the Rockey incision twice. In 1 patient, a ruptured appendix with abscess formation was encountered in the sac of a strangulated femoral hernia approached through an inguinal incision. In the final case, the diagnosis was incorrect and a Hoag incision was made.

It is a notable fact that hernias did not occur in any McBurney incisions which were closed, whereas when such incisions were drained there were 8, or an incidence of 0.9 per cent, of 899 patients whose incisions were at this site. Of 18 cases of right rectus incisions, hernias developed in 2, an incidence of 11.1 per cent. In 10 cases of McBurney incisions with Weir extensions, there were 2 cases of evisceration and 3 of hernia. All the incisions were drained. Evisceration in the McBurney incisions was confined wholly to those with Weir extensions. This was 0.12 per cent, as compared with 0.65 per cent for all abdominal incisions<sup>10</sup> over a ten year period.

#### SURGEONS

The operations in this series were performed by thirty-nine surgeons, twenty of whom performed ten or more appendectomies.

#### CONSERVATIVE THERAPY

Conservative therapy in acute appendicitis with perforation has never been recommended at this clinic, although championed by others.<sup>11</sup> Thus, of 13 patients treated conservatively, 4 died after being admitted

8. Ladd, W. E., and Gross, R. E.: *Abdominal Surgery of Infants and Children*, Philadelphia, W. B. Saunders Company, 1941, p. 840.

9. Brett, J. D., and Watkins, R. M.: *McBurney Incision in Appendicitis*, Ohio State M. J. **39**:140 (Jan.) 1943.

10. Tashiro, S.: *Wound Disruption: A Study of 55 Cases at the Cincinnati General Hospital*, Surg., Gynec. & Obst. **78**:487 (May) 1944.

in terminal condition and 1 refused operation and recovered, while in 8 cases a resolving abscess was not drained although appendectomy was subsequently performed three to six months later.

In 32 cases appendectomy was not performed, in spite of exploratory operation, because the presence of the appendix in or beyond the confines of a well walled-off abscess precluded its removal. Six of the patients were readmitted for subsequent operation for interval appendicitis, and 1 returned after several months with acute appendicitis with perforation and generalized peritonitis.

#### DRAINAGE

In an earlier article, our views at that time concerning drainage in acute appendicitis with perforation were discussed at some length and can be summarized in this excerpt: ". . . unless extensive necrosis or actual fecal contamination of the peritoneal cavity is present it is better to close the peritoneum and drain the wound down to it."<sup>2</sup> Among the arguments for such a procedure are (1) wounds in which the peritoneal cavity has been drained are prone to hernias,<sup>12</sup> (2) drains form a portal of entry for infection from without, (3) drains are foreign bodies and may stimulate adhesions, which may result in intestinal obstruction, and (4) the obtaining of drainage from remote portions of the peritoneal cavity by drains<sup>13</sup> is unlikely.

The findings of the second and present reviews may force us to modify our previous policy. Granted that drains which are placed customarily in the pelvis and the right paravertebral gutter will not allow the escape of pus from more distant portions of the abdominal cavity, there is clinical evidence to show that an avenue has been established for the escape of pus localized at or contiguous to the areas in which the drains are placed. Thus in several cases it has been a satisfaction to observe subsidence of severe abdominal signs and symptoms as large quantities of exudate escaped from the drainage tract at the time of or even several days after the removal of the drains.

In the consideration of the complication of pelvic abscess, it has been noted that this condition occurs with greater frequency in the cases in which the peritoneum is closed and only the wound drained than in those in which the abdominal cavity is drained. Of 58 cases of

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11. Ochsner, A., cited by Reynolds, J. J.: Conservative Management of Appendiceal Peritonitis, *New Orleans M. & S. J.* **87**:32 (July) 1934. Adams, J. M., and Bancroft, P. M.: The Conservative Management of Appendiceal Peritonitis in Children, *J. Pediat.* **12**:298 (March) 1938. Reynolds.<sup>7a</sup>

12. Cave, H.: Incidence and Prevention of Incisional Hernias, *J. A. M. A.* **101**:2038 (Dec. 23) 1933.

13. Meleney, F. L., and Howes, E. L.: Disruption of Abdominal Wounds with the Protrusion of Viscera, *Ann. Surg.* **99**:5 (Feb.) 1934.

acute appendicitis with perforation in which the incisions were drained to the peritoneum, pelvic abscesses developed in 14, or 24.1 per cent, whereas this complication developed in only 21, or 12.1 per cent, of the 174 cases in which the peritoneal cavity was drained. In the 1934-1938 series the corresponding percentages were 12.73 and 9.1 respectively. On the other hand, in this series there remains a noticeable discrepancy in the mortality rate in the cases in which the incisions were drained down to the abdominal cavity and those in which the peritoneal cavity was drained, the respective mortality rates being 8.6 per cent and 12.1 per cent. In the preceding review a corresponding comparison was 9.1 per cent and 16.2 per cent respectively. It must be emphasized that drainage of the peritoneal cavity was dependent on the amount of "contact necrosis" and "fecal contamination."

Of 11 patients with acute appendicitis with perforation and peritonitis whose wounds were closed without drainage, infections developed in the incision in 7, or 63.8 per cent. There were in all 8 patients with appendicitis with perforation and abscess formation whose incisions were closed and in whom no complications arose. The remaining 9 patients with appendicitis with rupture were treated conservatively (table 1).

TABLE 1.—*Management of Wounds in Cases of Ruptured Appendixes*

|                                    | Number of Cases |
|------------------------------------|-----------------|
| Drainage of wound.....             | 58              |
| Drainage of peritoneal cavity..... | 74              |
| Closure without drainage.....      | 19              |
| Conservative treatment.....        | 9               |

In 25 cases of acute appendicitis without perforation drains were placed down to (8 cases) or into the peritoneum (17 cases) for various reasons, such as bleeding, contamination and suspected bacterial perforation. Pelvic abscesses did not occur in this group.

#### BACTERIOLOGY

Any exudate encountered in the peritoneal cavity at operation is cultured. The number of positive cultures and the varieties of organisms obtained were disappointing but not unexpected. Because of unavoidable curtailments in personnel, plating of swabs has been frequently delayed, with the result that many cultures which obviously should have been positive under normal conditions have been negative. Altmeier<sup>14</sup> has shown that a large number of the organisms recovered from the peritoneal cavity in cases of peritonitis are of the anaerobic type. During

14. Altmeier, W. A.: The Pathogenicity of the Bacteria of Appendicitis Peritonitis, *Surgery* **11**:347 (March) 1942; *Surgical Infections of the Peritoneum*, *S. Clin. North America* **22**:437 (April) 1942.

much of the period reported on in this study, the routine failed to provide for culture of this group of organisms.

#### DURATION OF HOSPITAL STAY

The average duration of hospitalization of patients with acute appendicitis without perforation was 9.25 days. The mean duration of hospitalization for patients with perforation and generalized peritonitis and perforation with abscess formation was 21.6 and 22.7 days respectively.

TABLE 2.—*Complications in Cases of Appendicitis*

|   | Chronic<br>or<br>Interval | Acute<br>Without<br>Perforation | Perforation<br>and<br>Peritonitis | Perforation<br>and<br>Abscess | Total |
|---|---------------------------|---------------------------------|-----------------------------------|-------------------------------|-------|
| Atelectasis.....                                | 0                         | 4                               | 7                                 | 1                             | 12    |
| Reaction to blood transfusion..                 | 1                         | 0                               | 1                                 | 0                             | 2     |
| Generalized peritonitis.....                    | 0                         | 1                               | ..                                | 2                             | 3     |
| Pulmonary edema.....                            | 0                         | 0                               | 2                                 | 2                             | 4     |
| Paroxysmal tachycardia.....                     | 0                         | 0                               | 0                                 | 1                             | 1     |
| Uremia.....                                     | 0                         | 0                               | 0                                 | 2                             | 2     |
| Retroperitoneal abscess.....                    | 0                         | 0                               | 0                                 | 1                             | 1     |
| Cervical adenitis.....                          | 0                         | 1                               | 0                                 | 0                             | 1     |
| Sinus in wound.....                             | 0                         | 0                               | 2                                 | 2                             | 4     |
| Keloid.....                                     | 1                         | 4                               | 2                                 | 1                             | 8     |
| Acidosis.....                                   | 0                         | 0                               | 1                                 | 1                             | 2     |
| Erysipelas.....                                 | 0                         | 1                               | 0                                 | 0                             | 1     |
| Psychoneurosis.....                             | 0                         | 0                               | 0                                 | 1                             | 1     |
| Paronychia.....                                 | 0                         | 0                               | 0                                 | 1                             | 1     |
| Gangrene of ileum.....                          | 0                         | 0                               | 1                                 | 0                             | 1     |
| Portal thrombophlebitis.....                    | 0                         | 0                               | 1                                 | 0                             | 1     |
| Acute hemorrhage from cecum..                   | 0                         | 0                               | 1                                 | 0                             | 1     |
| Subphrenic abscess.....                         | 0                         | 1                               | 7                                 | 1                             | 9     |
| Pulmonary congestion.....                       | 0                         | 0                               | 0                                 | 1                             | 1     |
| Pelvic abscess.....                             | 0                         | 0                               | 30                                | 8                             | 38    |
| Subhepatic abscess.....                         | 0                         | 1                               | 0                                 | 1                             | 2     |
| Thrombophlebitis.....                           | 0                         | 1                               | 3                                 | 2                             | 6     |
| Fecal fistula.....                              | 0                         | 0                               | 5                                 | 3                             | 8     |
| Otitis media.....                               | 0                         | 1                               | 1                                 | 0                             | 2     |
| Empyema.....                                    | 0                         | 0                               | 4                                 | 0                             | 4     |
| Acute toxic leptomenigitis....                  | 0                         | 0                               | 1                                 | 0                             | 1     |
| Wound infection, clean patients                 | 0                         | 18                              | 0                                 | 0                             | 18    |
| Wound infection, dirty patients                 | 0                         | 0                               | 16                                | 4                             | 20    |
| Liver abscess.....                              | 0                         | 0                               | 1                                 | 0                             | 1     |
| Evisceration.....                               | 0                         | 1                               | 1                                 | 0                             | 2     |
| Hernias.....                                    | 0                         | 3                               | 8                                 | 2                             | 13    |
| Jaundice.....                                   | 0                         | 4                               | 8                                 | 4                             | 16    |
| Pleural effusion.....                           | 0                         | 0                               | 5                                 | 0                             | 5     |
| Thyroid crisis.....                             | 0                         | 1                               | 0                                 | 0                             | 1     |
| Acute cholecystitis.....                        | 1                         | 0                               | 0                                 | 0                             | 1     |
| Dermatitis venenata.....                        | 0                         | 3                               | 0                                 | 0                             | 3     |
| Lobar pneumonia.....                            | 0                         | 0                               | 1                                 | 0                             | 1     |
| Complications in urinary tract..                | 0                         | 4                               | 1                                 | 1                             | 6     |
| Cerebral accident.....                          | 1                         | 0                               | 0                                 | 0                             | 1     |
| Soft tissue abscess.....                        | 0                         | 4                               | 1                                 | 1                             | 6     |
| Acute exacerbation rheumatic<br>valvulitis..... | 1                         | 0                               | 0                                 | 0                             | 1     |

#### COMPLICATIONS

As was done in the preceding survey, we content ourselves with listing the complications occurring with the various types of appendicitis, since there is no space for detailed discussion and no unusual conditions were encountered (table 2).

## MORTALITY

In accordance with the second paper of the series<sup>2</sup> the mortality statistics are based on all cases of appendicitis rather than on the operative cases, as in the initial study. The total number of deaths in the present series of 936 cases was 31, or 3.3 per cent, as compared

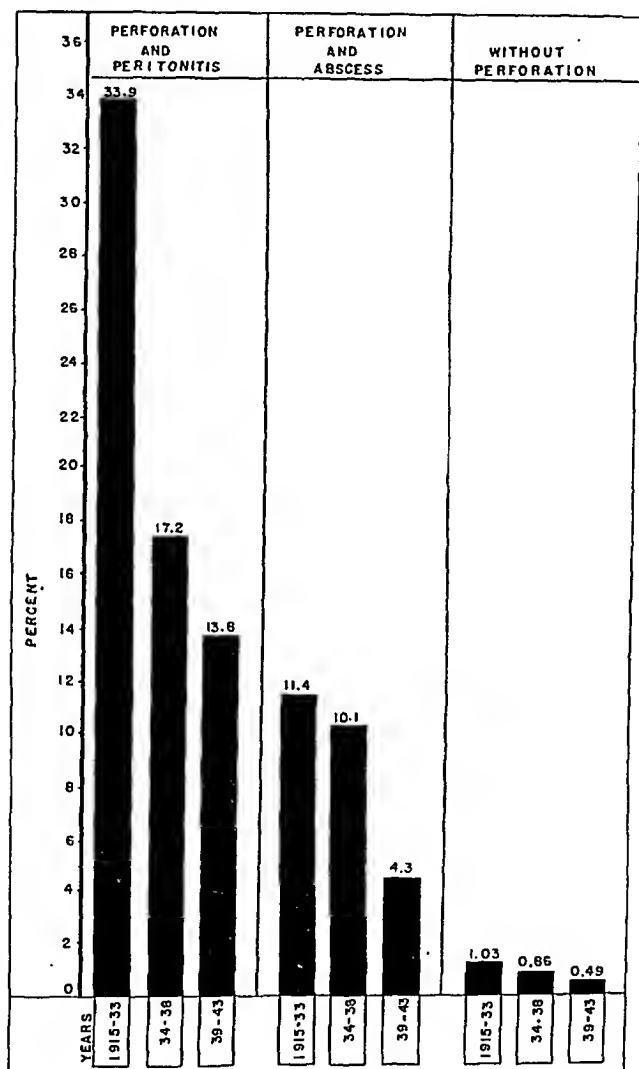


Chart 4.—Fatality rate in cases of acute appendicitis.

with 6.4 per cent and 4.86 per cent in the earliest and second reports respectively. In the group of cases classified as chronic or interval appendicitis, there was 1 death in 71 cases, a mortality of 1.4 per cent. The nature of the man's death (cerebral thrombosis) can hardly be ascribed to appendicitis. There were 3 deaths, 0.49 per cent, in the

group classed as acute appendicitis without perforation, against percentages of 0.86 and 1.03 for the first and second reviews.

In the group of 167 cases designated acute appendicitis with perforation and generalized peritonitis, 23, or 13.77 per cent, of the patients died, as compared with the respective figures 33.9 per cent and 17.2 per cent for the 1915-1933 and 1934-1938 series. Only 4, or 4.3 per cent, of 93 patients suffering with perforation and abscess formation died, in comparison with 11.4 per cent and 10.1 per cent for the first and second studies (chart 4).

TABLE 3.—*Mortality Based on Time Elapsed Between Onset of Symptoms and Admission*

|                     | Total Cases | Deaths | Per Cent |
|---------------------|-------------|--------|----------|
| 0 to 48 hours.....  | 659         | 14     | 2.1      |
| 49 to 72 hours..... | 97          | 4      | 4.1      |
| 73 to 96 hours..... | 30          | 3      | 10.0     |
| 4 to 6½ days.....   | 41          | 6      | 14.6     |
| 6½+ days.....       | 34          | 3      | 8.8      |

The highest mortality occurred in the patients who delayed hospitalization. Thus, if the period between onset of symptoms and admission to the hospital is divided into five arbitrary groups, 2.1 per cent of the 639 patients who entered the hospital within forty-eight hours after the onset of symptoms died, whereas 10 per cent of the patients who

TABLE 4.—*Mortality and Cause of Death*

| Type of Appendicitis                        | Number of Cases | Total |
|---|-----------------|-------|
| Chronic and Interval.....                   |                 | 1     |
| Cerebral accident.....                      | 1               |       |
| Acute unruptured.....                       |                 | 3     |
| Thyroid crisis.....                         | 1               |       |
| Generalized peritonitis.....                | 1               |       |
| Death from anesthetic.....                  | 1               |       |
| Acute with perforation and peritonitis..... |                 | 23    |
| Generalized peritonitis.....                | 17              |       |
| Peritonitis and lobar pneumonia.....        | 1               |       |
| Peritonitis and bronchopneumonia.....       | 1               |       |
| Peritonitis and perforation of ileum.....   | 1               |       |
| Bronchopneumonia.....                       | 1               |       |
| Septicopyemia.....                          | 1               |       |
| Intra-abdominal abscesses (empyema).....    | 1               |       |
| Acute with perforation and abscess.....     |                 | 4     |
| Pulmonary edema.....                        | 1               |       |
| Generalized peritonitis.....                | 2               |       |
| Bronchopneumonia.....                       | 1               |       |

entered on the third and fourth day of their illness died. For a detailed presentation of the correlation between elapsed time between onset of symptoms and admission and death table 3 is available.

#### CAUSE OF DEATH

It will be unnecessary to elaborate on the cause of death in the 31 fatal cases, since they are listed in table 4.



It is perhaps fitting to comment that of the 4 deaths listed under the first two groups only 1 was due to intra-abdominal pathologic changes.

#### CHEMOTHERAPY

Since the publication of the last review, the surgical treatment of appendicitis has been supplemented by chemotherapy. (Penicillin was not used in any case of appendicitis included in this report.) The present medical literature throngs with excellent articles on the use of sulfonamide compounds in abdominal operations. At present the consensus is that intraperitoneal administration of sulfone preparations has a definite and advantageous place in abdominal operations,<sup>15</sup> although there is a tendency to replace it by general administration by other parenteral routes.

It is needless to state that the patients in the earlier cases in this series who were given sulfone compounds did not receive uniform management. Such variations are expected with the advent of a new therapeutic agent. In recent months the management has been standardized to a fair degree. At present, chemotherapy is reserved only for the patients with generalized peritonitis or those in whom its onset is feared. For example, the patients with perforation and abscess formation in whom there is a possibility of extension with resultant generalized peritonitis and those with acute appendicitis without rupture but with contiguous cellulitis, necrosis or possible bacterial perforation are given chemotherapy. At operation (in adult patients) 5 Gm. of sulfanilamide are placed in the peritoneal cavity just before closure. Postoperatively the dose is supplemented by sulfadiazine or its sodium salt in quantities necessary to obtain and maintain a blood level of 8 to 12 mg. per hundred cubic centimeters for as long a period as indicated by the clinical course. Frequent estimates of blood sulfone levels, urinalyses and blood counts help to minimize the possibility of overdosage. Serious complications did not result from the use of sulfonamide drugs. Jaundice was noted in 5 cases, while there was no record of oliguria, anuria, gross hematuria or agranulocytosis. Of 865 patients with acute appendicitis, perforative or nonperforative, 181 received sulfone preparations for the treatment of the primary disease. (Patients who received chemotherapy for complications of appendicitis were not considered.)

15. (a) Waugh, J. M.; McCall, C. H., and Herrell, W. E.: Intraperitoneal Chemotherapy, *S. Clin. North America* **23**:1144 (Dec.) 1943. (b) Intraperitoneal Administration of Sulfanilamide, editorial, *J. A. M. A.* **119**:796 (July 4) 1942. (c) Jackson, A. S.: Chemotherapy in Adjunct to Surgery with Report of Use of Sulfathiazole Intraperitoneally, *South. Surgeon* **11**:274 (April) 1942. (d) Anglem, T. J., and Clute, H. M.: The Intraperitoneal Use of Sulfanilamide in Gastrointestinal Resections, *New England J. Med.* **229**:432 (Sept. 9) 1943.

In only one group, acute appendicitis with perforation and generalized peritonitis, was the use of sulfonamide compounds of demonstrable value. Of the 167 patients in that group, 114 received sulfonamide drugs, with a mortality rate of 11.3 per cent (13 deaths) as compared with 18.8 per cent (10 deaths) in 53 untreated patients. In 1943 there were no deaths in the class designated perforation and peritonitis, and all the 38 patients had received chemotherapy.

The mortality of the 93 patients with appendicitis and abscess formation was 4.5 per cent and 4.1 per cent respectively for the groups of treated and untreated patients. This difference is too small to be significant. The incidence of postoperative complications and the duration of hospitalization were not grossly influenced by the use of chemotherapy.

#### SUMMARY

This study shows that there has been a further pronounced reduction of the incidence of acute appendicitis with perforation.

A secondary effect of the decreased incidence of perforation has been the striking rise in the number of cases of acute appendicitis without perforation. That this increase was achieved at the expense of the other groups is evidenced by the fact that it is an absolute increment occurring in spite of a 19 per cent reduction in the total number of cases as compared with that of the previous study.

It would seem important to stress that appendicitis as seen in patients of middle years must be differentiated from conditions which are uncommon in younger patients. Perforation occurred in 58 per cent of the patients with acute appendicitis who were over 40 years.

Since the advent of the educational campaign directed by the Public Health Federation and the Academy of Medicine of Cincinnati, the use of cathartics and the delay in hospitalization have been substantially reduced.

A striking illustration of the successful results of this campaign is drawn from a comparison of our statistics with those of another clinic.

In that study <sup>6a</sup> 1,680 consecutive cases of appendicitis were reviewed. The patients were drawn from a population of 350,000 who lived in an area of 3 square miles (8 sq. km.). The citizens were informed by "various social and medical groups" as to the dangers of catharsis and procrastination with the presence of abdominal pain. There were four hundred and sixteen physicians in this area. Of 1,680 patients, 57.7 per cent were operated on within twenty-four hours after the onset of symptoms and 77.1 per cent within forty-eight hours. Only 41 per cent could be considered charity patients.

In contrast the community of Cincinnati sprawls over 72 square miles (185 sq. km.). The population is 455,610; yet 70.1 per cent of all patients with appendicitis in a 100 per cent charity institution

were hospitalized within forty-eight hours after the onset of symptoms. We anticipate a further improvement in the next review.

In the previous report it was stated that "unless extensive necrosis or actual fecal contamination of the peritoneal cavity is present it is better to close the peritoneum and drain the wound down to it." Our statistics show that this practice may need to be modified. As in the 1934-1938 series, the incidence of postoperative pelvic abscess formation in patients thus treated was significantly greater. There was no striking difference in the mortality rates of patients in whom the wounds were drained to the peritoneum (8.6 per cent) or in whom the peritoneal cavities were drained (12.1 per cent).

There was a further decrease in the mortality rate from appendicitis during the past five years. In a recent paper by Groom,<sup>16</sup> the author noted that "all sections of the country have experienced decreases in appendicitis mortality since 1930. Twenty states had reductions of 60-70 per cent, 20 other states had reductions of 50-60 per cent. The death rate from appendicitis among Metropolitan Life Insurance Industrial Policyholders dropped from 14.4 per 100,000 in 1929 to 5.2 in 1943, a decline of 64 per cent. The resident death rate in Cincinnati (from appendicitis) dropped from 18.4 per cent in 1929 to 4.9 per cent in 1943, a decline of 74 per cent."

In 1929 the death rate from appendicitis in Cincinnati was the second highest of any large city in the country. In the succeeding years intensive effort, for the most part voluntarily and gratuitously given, achieved striking results. "Newspapers, radio, car and bus cards, posters, leaflets, cards and circulars, window exhibits, talks and lectures in schools and at public meetings were employed. Physicians were also bulletined (on the subject) at intervals through the Academy of Medicine."<sup>16</sup> The most convincing testimony as to the effectiveness of this campaign is found in the data submitted by Groom. From its unenviable position as the city with one of the highest death rates from appendicitis in 1929, the city of Cincinnati had the lowest average resident death rate in 1939-1941 from appendicitis of thirteen cities of comparable size chosen at random.

There are some who would attribute the reduced mortality from appendicitis entirely to the sulfone compounds. In our experience chemotherapy has undoubtedly benefited a single group, namely, patients with perforation and peritonitis. An accurate assay of the role played by chemotherapy in the reduction of the death rate from appendicitis is not possible at this time. There are reports<sup>17</sup> that sulfonamide drugs are a major factor in the improvement. We think it only appropriate

16. Groom, W. S.: A Comparative Study of Mortality 1929-1943 Inclusive—Appendicitis, Public Health Federation of Cincinnati, June 1944.

17. Brett and Watkins.<sup>9</sup> Jackson.<sup>15c</sup>

to emphasize that in this clinic <sup>3</sup> as in others <sup>15a</sup> there has been a steadily decreasing mortality rate from appendicitis which preceded the advent of chemotherapy and that it has not been radically altered by their use.

In the earlier studies sufficient attention was not directed toward certain aspects of appendicitis in the Negro race. A careful study of the statistics indicates that in spite of the imposing results in the educational campaign a certain underprivileged minority has not received the maximum possible benefit from the measures employed. A certain degree of illiteracy, a lower economic status, a lack of telephones and transportation and relatively fewer physicians or interested influential

TABLE 5.—*Comparative Observations on Appendicitis in White and Negro Patients*

|   | White       |                                   | Negro       |                                   |
|---|-------------|-----------------------------------|-------------|-----------------------------------|
|   | Number of   | Per Cent of                       | Number of   | Per Cent of                       |
| Acute appendicitis; incidence of perforation          | Cases       | Cases                             | Cases       | Cases                             |
| Total number of cases.....                            | 637         |                                   | 228         |                                   |
| Cases with perforation.....                           | 173         | 27.2                              | 87          | 38.2                              |
| Delay in hospitalization for acute appendicitis       |             |                                   |             |                                   |
| Cases without perforation.....                        | 461*        | 26.4                              | 141         | 30.3                              |
| Cases with perforation.....                           | 173         | 74.0                              | 86†         | 81.9                              |
| Cathartics in cases of acute appendicitis             | Number      | Number Taking Cathar-tics         | Number      | Number Taking Cathar-tics         |
| Cases without perforation.....                        | 464         | 135                               | 141         | 64                                |
| Cases with perforation.....                           | 173         | 89                                | 87          | 51                                |
|   |             | Per Cent of Total                 |             | Per Cent of Total                 |
|   |             |                                   |             |                                   |
|   | Number      | Number Taking These Com-pounds    | Number      | Number Taking These Com-pounds    |
| Type of cathartic                                     |             |                                   |             |                                   |
| Magnesium sulfate or castor oil                       | 637         | 83                                | 228         | 71                                |
|   |             | Per Cent of Deaths in Total Cases |             | Per Cent of Deaths in Total Cases |
| Mortality   | Total Cases | Deaths                            | Total Cases | Deaths                            |
| All appendicitis, including chronic and interval..... | 692         | 18                                | 244         | 13                                |
|   |             | 59.1                              |             | 41.9                              |

\* In 3 cases elapsed time not known.

† In 2 cases elapsed time not known.

citizens are factors which well may restrict the efficiency of the campaign described by Groom. The extremely discouraging observations made on appendicitis in the Negro race are listed in table 5. It is found that perforation is 11 per cent commoner in the Negro race. The elapsed time before hospitalization is approximately four to eight hours longer in the groups of cases of acute appendicitis without perforation and with perforation. Among Negroes catharsis is 18.2 per cent more frequent in acute appendicitis and almost 7 per cent commoner in the group in which perforation has occurred. The use of the more violent cathartics (castor oil and magnesium sulfate as examples) is 16.5 per

cent commoner in the Negro race. Finally, the mortality rate in 244 cases of appendicitis in Negro patients was 5.32 per cent (13 of 244 cases) as compared with 2.6 per cent (18 deaths in 692) in white patients. Expressed in another manner, although only 26 per cent of the patients with appendicitis were Negroes 41.9 per cent of the deaths from appendicitis occurred in that race.

#### CONCLUSIONS

1. The cases of 936 patients with appendicitis who entered the Cincinnati General Hospital in 1939 to 1943 inclusive are reviewed. This article is the third of a series which began with a review of all cases of patients with appendicitis admitted to this institution since 1915 and which will be continued at five year intervals.

2. The incidence of chronic and interval appendicitis was greatly decreased in this five year period. Seventy-one cases, or 7.5 per cent of the total, belong to this group (1934-1938: 232 cases, or 20.1 per cent). This reduction is explained by more stringent criteria imposed on the classification of this group. The incidence of acute appendicitis without perforation showed an absolute and relative increase, 605 cases, or 70 per cent, in comparison to 582 cases, or 63.3 per cent, in 1934-1938. The incidence of perforation in acute appendicitis showed a decrease, 260 cases, or 30 per cent, as against 338 cases, or 36.7 per cent, in 1934-1938.

3. Perforation occurred in 58 per cent of all cases of acute appendicitis in patients over 40 years.

4. Cathartics were employed by 38.3 per cent of all patients with acute appendicitis (1934-1938: 44.5 per cent).

5. The average delay in hospitalization in acute unruptured appendicitis was 26.6 hours, well under the mean of 33.1 hours in 1934-1938. In perforation with acute appendicitis, the average delay in hospitalization was 75.6 hours, almost twenty-five hours less than the mean of one hundred hours in the last study.

6. There has been considerable discussion concerning the operative management of acute appendicitis with perforation. When the two five year periods are combined, analysis shows that the serious complication of pelvic abscess occurred in 33 of a total of 304 patients (10.8 per cent) in whom the peritoneal cavity was drained. This included drains into the pelvis as well as the right paravertebral gutter. On the other hand, there were 21 among 113 patients (18.5 per cent) in whom the peritoneum was closed and only the wound was drained. Thus it is seen that the frequency of this complication was greater when the peritoneal cavity was not drained. However, in this ten year period it is only fair to point out that in these same two groups the mortality

rate was 13.8 per cent with intra-abdominal drainage and 8.8 per cent with drainage of the wound alone. However, it should be stressed that the patients with peritoneal drainage were usually much sicker at the onset than those without peritoneal drainage and also that there were 304 cases in the former group and only 113 cases in the latter group.

7. The reduction in mortality from appendicitis may be attributed at least in part to an intensive educational campaign begun in 1934, at which time Cincinnati's death rate from appendicitis was among the highest of those in large cities in the United States. A recent survey demonstrates Cincinnati's mortality rate from appendicitis in 1943 to be among the lowest of those in thirteen cities of comparable size and racial composition.

8. The exact role of sulfone therapy in the reduced mortality rate cannot be determined at this time, because of insufficient data. Chemotherapy seemed to be of assistance in the group of cases classed acute appendicitis with perforation (mortality 13.77 per cent against 17.22 per cent in 1934-1938). The next survey from this clinic will be based on sufficient data to enable a more comprehensive estimate of the value of sulfonamide therapy.

9. Appendicitis as seen in the Negro race is a disease of severer proportions than that in the white race. The mortality rate is 5.3 per cent as against 2.6 per cent among white patients. Deaths among Negro patients (13) composed 41.9 per cent of the deaths for the entire series. Should the educational campaign be more effectively focused on this group, a significant improvement in the morbidity and mortality rate of appendicitis in the Negro race may be expected.

## TREATMENT OF POISONING WITH RATTLESNAKE VENOM

Experiments with Negative Pressure, Tourniquet and Bulb Suction

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AND

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**D**URING the first decade of this century the use of serums (antivenin) in the treatment of snake bite became widespread, and investigation of other methods came almost to a standstill. Limited effectiveness, high cost and allergy to large quantities of horse protein are serious handicaps to the use of serum. For this reason the continued investigation of other therapeutic measures, such as mechanical extraction of venom by various types of suction, is highly advisable.

Experiments by Dr. Dudley Jackson<sup>1</sup> and co-workers have proved that venom of the Texas diamond-backed rattlesnake (*Crotalus atrox*) can be removed locally for many hours after injection of the venom by restricting absorption with a tourniquet and applying suction to cruciate incisions made in the neighborhood of the bite.

In perusing papers by Jackson and others, we became interested in the possibility of developing a better method for extracting venom by suction and also in determining just what part of Jackson's results could be attributed to constriction by the tourniquet and what part to suction. A study of the literature failed to reveal any reports on the use of a tourniquet alone except in Australia, where Fairley<sup>2</sup> got only negative results in working with the effects of elapid venom on sheep. Even when he used Russell's viper (*Vipera russelii*) venom in relatively small amounts (less than two minimum lethal doses) his results were largely negative.

We designed our experiments to test the relative efficacy of three forms of local therapy, used individually and in combination: (1) nega-

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These experiments were performed in the Department of Surgery, University of Illinois College of Medicine. Dr. Warren H. Cole, Head of the Department of Surgery, gave many helpful suggestions. Valuable technical assistance was rendered by Mr. Everett Hoppe and Mr. Wilmer Eigsti.

1. (a) Jackson, D.: First Aid Treatment for Snake Bite, Texas State J. Med. **23**:203, 1927. (b) Jackson, D., and Harrison, W. T.: Mechanical Treatment of Experimental Rattlesnake Venom Poisoning, J. A. M. A. **90**:1928 (June 16) 1928. (c) Jackson, D., and Githens, T. S.: Treatment of *Crotalus Atrox* Venom Poisoning in Dogs, Bull. Antiven. Inst. America **5**:1, 1931.

2. Fairley, N. H.: Criteria for Determining the Efficacy of Ligature in Snake Bite, M. J. Australia **1**:377, 1929.

tive pressure, (2) the tourniquet and (3) suction as applied by Jackson. The first of these is new.

## EXPERIMENTAL METHODS

All the venom used in our experiments had been milked from Texas diamond-backed rattlesnakes (*Crotalus atrox*) at Ross Allen's Reptile Institute, Ocala, Fla. The venom, received in desiccated form, was prepared for use by dissolving the desired amount in from 1 to 2 cc. of distilled water. The dogs were anesthetized with intraperitoneal injections of 3 per cent pentobarbital sodium in the dose of 0.5 cc. per pound (0.5 Kg.) of body weight. We used the previously calculated<sup>1a</sup>

TABLE 1.—*Treatment by Alternating Negative Pressure*

| Negative Pressure (mm. Hg) and Duration, Minutes   | Number of Minimum Lethal Doses Injected | Weight of Dog, Lb. | Type and Number of Incisions; Interval Before Incisions  | Amount of Fluid Extracted, Cc. | Results              |
|--|---|--------------------|--|--------------------------------|----------------------|
| 120 for 10<br>400 for 10<br>120 for 15<br>60 for 5 | 3                                       | 22                 | Cruciate incision at site of injection and ring-cut above 15 min. after injection *                | 130                            | Survived             |
| 120 for 10<br>60 for 10<br>Alternately for 1 hour  | 8                                       | 22                 | Cruciate incision at site of injection 30 min. after injection †                                   | 120                            | Survived             |
| 120 for 10<br>60 for 10<br>Alternately for 1 hour  | 8                                       | 15                 | Cruciate incision at site of injection 35 min. after injection *                                   | 85                             | Survived             |
| 120 for 10<br>60 for 5<br>Alternately for 1 hour   | 8                                       | 47                 | Cruciate incision at site of injection 30 min. after injection *                                   | 233                            | Survived             |
| 120 for 8<br>60 for 2<br>Alternately for 1 hour    | 8                                       | 19                 | Incision made at site of injection 30 min. after injection *                                       | 155                            | Died in 42 hr.       |
| 120 for 8<br>60 for 2<br>Alternately for 1½ hours  | 8                                       | 12                 | Cruciate incision at site of injection 30 min. after injection; 2 more made 1 hr. after first *    | 82                             | Died in 24 to 48 hr. |
| 120 for 8<br>60 for 2<br>Alternately for 1½ hours  | 8                                       | 15                 | 5 puncture-like cruciate incisions made 20 min. after injection; 2 more made 1 hr. after the 5th † | 50                             | Died in 24 hr.       |

\* Negative pressure applied immediately after incision.

† Negative pressure not applied until 20 minutes after incision because of difficulty in arresting excessive bleeding.

‡ Negative pressure not applied until 10 minutes after incision.

minimum lethal dose of venom for dogs, which is 1 mg. of desiccated venom for every pound (0.5 Kg.) of the dog's weight. The venom was always injected subcutaneously on the outside of the dog's hindleg, about halfway between the ankle and the knee.

Using 9 dogs, Jackson established the minimum lethal dose of venom injected subcutaneously as 1 mg. for each pound of body weight. All the dogs died in five days. We checked this minimum lethal dose with 7 dogs, of which 2 died in twenty-four hours, 1 in forty-eight and 1 in seventy-two. Three other dogs given injections of two, three and eight minimum lethal doses died in seventy, twenty-two and twenty-three hours respectively.



*A. Negative Pressure Experiments.*—The apparatus necessary for the experiment was a large-mouthed glass bottle with a screw top. An oval opening in this metal top was surrounded by a metal cuff into which a dog's leg would fit snugly. Petrolatum and a strip of rubber dam served to make a moderately airtight connection between leg and cuff. There were two connections to the apparatus, one through which the negative pressure was applied by a suction pump and the other for measurement of the pressure with a manometer. A calculated amount of snake venom was injected into the dog's leg and, after half an hour, several cruciate (1 cm.) incisions were made through the skin of the area previously receiving the snake venom and the limb inserted into the suction bottle. This apparatus would probably be available only at hospitals, and it would take the patient at least thirty minutes to get to the nearest hospital. Therefore, thirty

TABLE 2.—*Treatment by Tourniquet*

| Number of Cases | Number of Minimum Lethal Doses Given Each Dog | Weight of Dog, Pounds | Interval Before Applying Tourniquet, Minutes | Duration of Constriction, Hours | Results: Survived Injection, Hours § |
|-----------------|---|-----------------------|--|---------------------------------|--------------------------------------|
| 1               | 4   | 24                    | None   | 23                              | 144                                  |
| 1               | 4   | 25                    | None   | 8-18                            | 144                                  |
| 2               | 4   | 17, 22                | 3-5  | 17½                             | 162                                  |
| 1               | 4   | 17                    | 3-5  | 17½                             | 138                                  |
| 1               | 4   | 21                    | 3-5  | 17½                             | 18 *                                 |
| 2               | 6   | 18, 24                | None   | 6                               | 144                                  |
| 2               | 6   | 10, 18                | 1  | 17                              | 137                                  |
| 1               | 6   | 11                    | 1  | 16½                             | 69                                   |
| 1               | 6   | 12                    | 1  | 17                              | 17 †                                 |
| 1               | 8   | 13                    | None   | 4                               | 144                                  |
| 2               | 8   | 10, 14                | None   | 5, 6                            | 23                                   |
| 1               | 8   | 13                    | None   | 5¼ †                            | 23                                   |
| 1               | 8   | 19                    | None   | 5½ †                            | 72                                   |
| 1               | 8   | 15                    | None   | 5¾ †                            | 120                                  |
| 3               | 8   | 16, 21, 24            | 5  | 19                              | 162                                  |
| 1               | 8   | 12                    | 1  | 18                              | 168                                  |
| 1               | 8   | 12                    | 1  | 18                              | 114                                  |
| 1               | 8   | 13                    | 1  | 18                              | 90                                   |
| 1               | 8   | 7                     | 1  | 18                              | 42                                   |
| 1               | 8   | 26                    | 5  | 19                              | 19                                   |

\* Dog probably died from combined effects of venom and distemper.

† Dog sensitive to pentobarbital sodium; probably died from combined effects of venom and pentobarbital sodium.

‡ Tourniquet pressure alternated between 120 mm. Hg for nine minutes and 60 mm. Hg for one minute during the first 1½ hours of treatment.

§ Many of these dogs were killed because of serious secondary infection.

minutes was allowed to elapse before application of negative pressure, which was then exerted on the leg for a period of one hour, alternating between 60 and 120 mm. of mercury. Variations were made as to time and pressure on the 7 dogs, as set forth in table 1.

*B. Tourniquet Experiments.*—To evaluate the benefit obtained from the various parts of Jackson's combined therapy,<sup>1</sup> we devised a group of experiments using only the tourniquet. After the venom had been injected into the anesthetized dog the tourniquet was applied proximal to the site of injection. It was not placed tightly enough to interrupt arterial flow but merely to obstruct venous and lymphatic return, and it was left in place from four to twenty-three hours. The procedure was carried out on a total of 26 dogs, as shown in table 2. Little or no time was allowed to elapse after injection of the venom, because we felt that this type of treatment would be available without loss of time to any person exposed to snake bites.

*C. Suction Experiments.*—Our third group of experiments was designed to test the efficacy of suction (as applied by cupping) to numerous 1 cm. cruciate incisions over the site of injection of venom. This form of therapy was applied to 4 dogs receiving injections of three, four and eight minimum lethal doses of snake venom, as shown in table 3.

*D. Tourniquet and Suction Experiments.*—The fourth type of experiment was performed on only 2 dogs. On these we combined the tourniquet with suction by cupping, as shown in table 4.

TABLE 3.—*Treatment by Bulb Suction (Without Tourniquet)*

| Number of Minimum Lethal Doses Injected | Weight of Dog, Lb. | Type and Number of Incisions; Interval Before Incisions  | Type and Duration of Suction; Interval Before Application of Tourniquet                                      | Results                    |
|---|--------------------|--|--|----------------------------|
| 3                                       | 18                 | Cruciate incision at site of injection made at once; 4 additional incisions made later                   | Suction begun at once after making first cut, and continued 4 hr.; 2 bulbs used alternately on multiple cuts | Survived                   |
| 4                                       | 12                 | Cruciate incision at site of injection made at once; 4 additional incisions made later                   | Suction begun at once after making first cut, and continued 4 hr.; 2 bulbs used alternately on multiple cuts | Survived                   |
| 8                                       | 18                 | Cruciate incision at site of injection made 5 minutes after injection; 6 additional incisions made later | Suction begun at once after making first cut, and continued 2 hr.; 3 bulbs used alternately on multiple cuts | Died in less than 24 hours |
| 8                                       | 21                 | Cruciate incision at site of injection made 5 minutes after injection; 2 additional incisions made later | Suction begun at once after making first cut, and continued 2 hr.; bulbs used alternately on multiple cuts   | Died in less than 24 hours |

TABLE 4.—*Treatment by Tourniquet and Bulb Suction*

| Number of Minimum Lethal Doses Injected | Weight of Dog, Lb. | Type and Number of Incisions; Interval Before Incisions             | Type and Duration of Ligation   | Type of Suction        | Results            |
|---|--------------------|---|---|------------------------|--------------------|
| 8                                       | 14                 | Cruciate incision at site of injection made 30 min. after injection | Tourniquet applied for 1 hr. at 120 mm. Hg for 10 min. and then 60 mm. for 10 min.              | Single bulb used 1 hr. | Died within 72 hr. |
| 8                                       | 32                 | Cruciate incision at site of injection made 30 min. after injection | Pressure of tourniquet alternated for 1 hr. between 120 mm. Hg for 9 min. and 60 mm. for 1 min. | Single bulb used 1 hr. | Survived           |

## RESULTS OF EXPERIMENTS

*A. Negative Pressure.*—The first 4 dogs subjected to the negative pressure treatment, with the affected limb in a suction bottle as described, survived. Three of these dogs had been given injections of eight and the fourth of three minimum lethal doses of venom. Three additional dogs (receiving eight minimum lethal doses) died in spite of therapy; their survival time was no longer than that in the control animals. The

mortality rate of dogs receiving eight minimum lethal doses of venom and subjected to this form of treatment was therefore 50 per cent, as shown in table 1.

*B. The Tourniquet.*—Table 2 gives the details and results of twenty-six experiments in which the tourniquet was the only form of therapy. Nineteen of the dogs given injections of four, six or eight minimum lethal doses of venom survived seventy-two hours or more. Survival for this length of time was interpreted as protection against the venom; it was necessary to kill many of these animals at the time because of secondary infection which developed in the ulcers produced by the local necrotizing effect of the venom. By this form of treatment, the mortality was reduced to 17 per cent when four and six minimum lethal doses of venom were injected and to 36 per cent when eight minimum lethal doses were given.

*C. Suction.*—Having investigated the effects of constriction by tourniquet, we felt it imperative to determine the value of suction alone. Jackson has already reported ten suction experiments with successful results on dogs that had received one to four and a half minimum lethal doses of *Crotalus atrox* venom. Our 2 dogs given injections of three and four minimum lethal doses survived with this form of therapy, whereas the 2 receiving eight minimum lethal doses died.

*D. Tourniquet and Suction.*—With the efficacy of the tourniquet and the suction treatment proved, it is reasonable to assume that the combination of the two would be better than either alone. Only 2 dogs were used in this group of experiments; 1 of them died from effects of the venom, as shown in table 4.

#### SUMMARY AND CONCLUSIONS

The survival of 4 out of 7 dogs treated by alternating negative pressure is evidence that the negative pressure method has possibilities; it would appear to be the most effective way to extract the venom. Impracticability is the chief drawback to this method. This drawback is not so serious if the method proves to be appreciably better than others that also call for hospital treatment. Rubber or glass boots (Pavex boot) for the application of alternating and negative pressure are standard equipment in many hospitals and can be adapted for this treatment. Further investigations of negative pressure are indicated.

The tourniquet experiments prove beyond doubt that moderately tight constriction above the site of injection of the venom greatly prolongs life and may even save it by slowing down the absorption of venom. Although the venom starts immediately to diffuse through the tissues and eventually travels up the lymphatic vessels to enter the systemic circulation, absorption is greatly retarded by the tourniquet.

Since the saving of life is probably accomplished at the cost of intensifying the local effects, constriction by tourniquet must be placed primarily in the category of first aid treatment. When competent medical aid is reached, the physician in charge will have to decide about continued use of the tourniquet.

Mild suction applied to cruciate incisions made over and through the site of injection of the venom extracts blood and serum that contain a high concentration of venom. This has been proved by injecting the exudate into another dog. Any venom extracted makes that much less for the body to detoxify and of course may mean the difference between life and death. Although suction has less practical value than has application of a tourniquet there are a limited number of bites on the head, neck and trunk that cannot be treated with a tourniquet.

In this group of experiments, the efficacy of antivenin was not tested, but there is evidence in other reports suggesting that it is by no means completely effective.

Our experiments supply additional evidence that application of a tourniquet (applied tightly enough to constrict flow of lymph and venous blood but not arterial), followed by mild suction over small cruciate incisions at the site of the snake bite, is an effective form of therapy, even when the quantity of venom is as great as eight minimum lethal doses.

# COMPARATIVE EFFICACY OF BLOOD FROM NORMAL AND FROM BURNED DONORS IN EXPERIMENTAL BURNS

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**E**FFORTS to explain the clinical course of patients receiving extensive superficial burns have led many clinicians to postulate the presence of a circulating toxin. Most of the experimental evidence presented in support of this view has been subject to the criticism that the treatment accorded the material removed from the burned animal might have contributed to its effect on the recipient. Since a simple transfusion of blood from a burned animal to a normal animal is generally well tolerated by the latter, it was decided to increase the possible sensitivity of the recipient to a hypothetical toxin by subjecting it, under ether anesthesia, to a standardized burn prior to the transfusion. The burn had been shown to result in a mortality of approximately 50 per cent in untreated animals. A second series of controls was employed, which was given transfusions of equivalent amounts of blood from normal animals.

## METHODS

Wistar rats were used as the test animals. All animals received a back burn of 32 per cent  $\pm 2$  of their total body surface by immersion in a water bath maintained at 90 C.  $\pm 0.25$  for fifteen seconds. The details of the method have been reported by McCarthy.<sup>1</sup>

For most experiments 12 stock rats, 6 weighing between 190 and 200 Gm. and 6 weighing between 200 and 210 Gm., were selected at random from stock cages. These again, by random selection, were divided into three groups of 4 in such a way that every group contained 2 animals in each weight range. After the burn, one group was infused with whole blood from burned rats, according to a method which will be described in detail later. Such blood is referred to in this paper as "postburn blood." One of the two remaining groups of 4 was infused with whole normal blood, and the third group served as the untreated controls.

The infusions of postburn and normal blood were in amounts based on 2 per cent of the body weight of the animals to be infused. They were given in all

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From the Harrison Department of Surgical Research, University of Pennsylvania Schools of Medicine.

1. McCarthy, M. D.: A Standardized Back Burn Procedure for the White Rat Suitable for the Study of the Effects of Therapeutic and Toxic Agents on Long Term Survival, *J. Lab. & Clin. Med.* 30:1027, 1945.

cases two hours following the burn and at the rate of 1.0 cc. per minute. The unanesthetized rats were tied on their backs to a restraining board. The infusions were given into the internal saphenous vein through a small incision in the skin. After the infusion the vein was compressed at the point of the needle puncture by a sterile sponge and then ligated above and below the site of puncture. Sterile topical thrombin was dusted into the cutaneous incision, which was then closed by two interrupted sutures. This procedure was found necessary to prevent bleeding from the site of injection and from severed capillaries of the skin due to the heparin content of the infused blood.

#### PREPARATION OF POSTBURN AND NORMAL BLOOD FOR INFUSION

Four hours after the burn the hematocrit values for rats receiving a burn of 45 per cent of the total body surface were about 140 per cent of the initial level. The viscosity of the blood from burned animals was such that it could be infused through a no. 27 gage needle only with great difficulty. To facilitate infusion and to obtain a cell-plasma ratio equivalent to that of the normal, the hematocrit level of the postburn blood was adjusted to 50 per cent by the addition of postburn plasma.

Postburn plasma was obtained by burning 4 large rats (300 to 400 Gm.) on the day preceding infusion. A 45 per cent  $\pm$  2 burn of the body surface produced an injury which invariably resulted in death within twenty-four hours. Four hours after the burn these animals were given 100 Toronto units of heparin (Connaught Laboratories) intravenously. Immediately thereafter, blood was withdrawn, by cardiac puncture, into a sterile 10.0 cc. syringe which had been wet with heparin solution. Approximately 3.0 cc. of blood was withdrawn from each rat; all samples were pooled in a 15.0 cc. graduated sterile centrifuge tube.

The same procedure being followed, blood was obtained from normal unburned animals and likewise pooled in a 15.0 cc. sterile centrifuge tube. Both postburn and normal blood were centrifuged for one-half hour at 2,500 rotations per minute. Great care was taken in removing the plasma to avoid contamination by the components that make up the buffy coat. The postburn plasma and the normal plasma thus prepared were placed in the freezing unit of an electric refrigerator in sterile containers and frozen.

Whole postburn blood and whole blood from normal animals were obtained in the same manner approximately sixteen hours before infusion and stored at 5 C.

On the day of the experiment the whole blood and plasma were brought to room temperature and then centrifuged for thirty minutes at 2,500 rotations per minute. A sufficient volume of stored postburn

plasma was then added to the whole postburn blood to give a 50 per cent hematocrit value.

In order to eliminate storage of part of the postburn plasma as an uncontrolled factor in the experiment, the normal whole blood was prepared by substitution of a like amount of stored normal plasma in it before it was infused. That is, after whole blood was drawn from normal animals, sixteen hours before the experiment, enough of the plasma was drawn off to raise the hematocrit level to that of the postburn blood. Stored normal plasma was then added to adjust the hematocrit level to 50.

### RESULTS

A total of 48 rats was used in the experiments, of which 16 rats each received a single infusion of 2 per cent of its body weight of whole

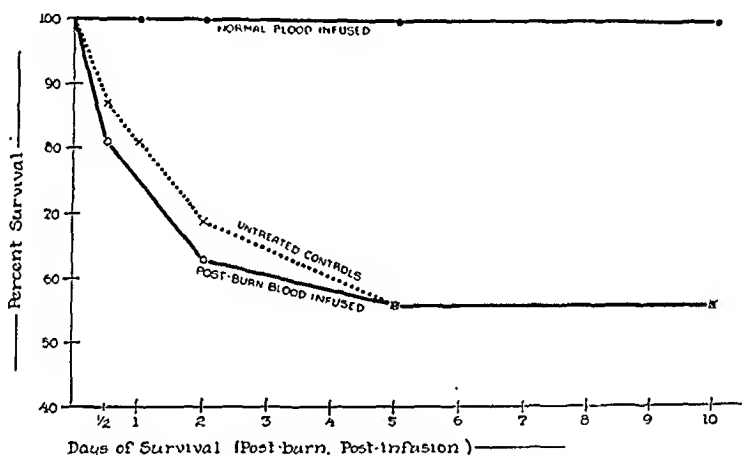


Chart 1.—The effect on survival of burned rats infused with normal and postburn blood.

postburn blood, 16 rats each received a single infusion of 2 per cent of its body weight of whole normal blood and 16 rats received no infusion.

Chart 1 shows the survival percentages of the three groups for a ten day period. A 56 per cent survival was obtained in the untreated group, and a 56 per cent survival occurred in the group receiving the postburn blood infusion. A 100 per cent survival was obtained in the group infused with normal whole blood. The survival of the normal blood group compared with that of the postburn blood and untreated control groups shows a highly significant difference on statistical analysis.

Hematocrit values expressed in per cent of the hematocrit value obtained before the burn are recorded in chart 2. The data are not well correlated with the survival rates of the different groups.

In view of the recent work of Tabor and Rosenthal,<sup>2</sup> which demonstrated a pronounced increased sensitivity to potassium changes in shocked animals, plasma potassium levels were determined on several samples of both normal and postburn blood prepared according to the technic described.

The Charnock and Montgomery method<sup>3</sup> being used, the average potassium level of the postburn plasma was 33.1 mg. per hundred cubic centimeters and that of the normal plasma was 30.5 mg. per hundred cubic centimeters. The increase of approximately 3.0 mg. per hundred cubic centimeters of potassium in the postburn plasma over that in the normal plasma, judging from Tabor and Rosenthal's<sup>2</sup> data, would hardly be sufficient in itself to explain the difference in survival between the two infusion groups. Hemoglobinemia was measured on the same

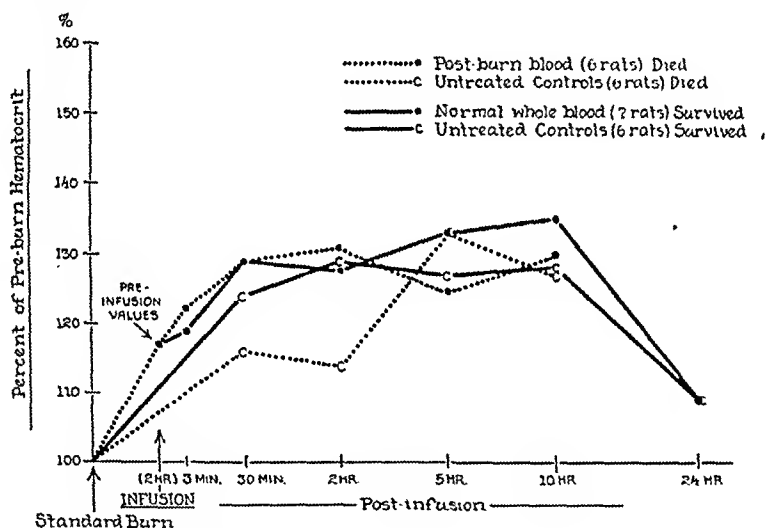


Chart 2.—Average hematocrit values of burned rats untreated and infused with normal and postburn whole blood.

samples by the spectrophotometric method. An average value of 75.0 mg. per hundred cubic centimeters was found in the normal plasma and an average of 407.0 mg. per hundred cubic centimeters in the postburn plasma.

In an effort to determine which of the constituents of the whole postburn blood was responsible for the decreased survival reported, a cellular suspension of cells from burned rats was prepared in isotonic solution of sodium chloride. These cells were obtained from postburn blood prepared as previously described. To the postburn cells was

2. Tabor, H., and Rosenthal, S. M.: Experimental Chemotherapy of Burns and Shock: VIII. Effects of Potassium Administration, of Sodium Loss and Fluid Loss in Tourniquet Shock, Pub. Health Rep. 60:373, 1945.

3. Charnock, F. W., and Montgomery, E. H.: Unpublished data.



added an equal volume of isotonic solution of sodium chloride. A similar suspension of normal red cells was simultaneously prepared. Twenty-four animals receiving the standardized 32 per cent burn described were infused with these two suspensions of red cells. Twelve animals received postburn cells in isotonic solution of sodium chloride, and 12 animals received normal cells in isotonic solution of sodium chloride. Eight of the 12 animals (66 per cent) which received the postburn cells survived, whereas 10 of the 12 animals (83 per cent) which received normal cells survived. There is no significant statistical difference in survival between these two groups, but both showed an increased survival over that of the untreated controls, which was 56 per cent. No significant differences in hematocrit values were observed between these two infusion groups or between the survivors or dead animals of either group. These results suggest that the changes induced in the blood of burned donors are likely to be found in the plasma. Further studies on the chemical alterations of postburn plasma are in progress.

#### COMMENT

Prior to the experiments reported here in detail we had confirmed the fact that a single transfusion of blood from a burned rat was not lethal to a normal rat in amounts up to 2 per cent of the body weight. It was felt that any attempt to extract or concentrate a toxic factor in the postburn blood might result in the production of new substances or in the concentration of normal constituents, such as potassium, in amounts which would be toxic. Therefore, the other alternative, of increasing the sensitivity of the test animal by producing a burn which yielded a standard mortality rate, was selected. The usefulness of this method depended on whether or not it would be possible to standardize a burn accurately enough to predict the mortality. The method evolved for this has been published by one of us (M. McC.), and, while it is affected to some extent by seasonal factors, we believe that it is reliable when controls are run simultaneously.

For several decades the possibility that thermal burns produce a toxic material which is distributed widely in body fluids has been considered. In 1923 Robertson and Boyd<sup>4</sup> reported experiments which seemed to support such a view. Their conclusions were questioned by Underhill and Kapsinow,<sup>5</sup> and by 1930 the interest of most investigators in this field was focused on the part played by the fluid and

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4. Robertson, B., and Boyd, G.: *Toxemia of Severe Superficial Burns in Children*, *Am. J. Dis. Child.* **25**:163 (Feb.) 1923.

5. Underhill, F. P., and Kapsinow, R.: *The Alleged Toxin of Burned Skin*, *J. Lab. & Clin. Med.* **16**: 823, 1931.

electrolyte shift in the burned patient. Underhill and his associates<sup>6</sup> have attributed all or most of the systemic disturbances of burns in the first few days following the burn to a combination of fluid and salt depletion of the blood. However, in 1937 Wilson, Jeffrey, Roxburgh and Stewart<sup>7</sup> reported that the protein-containing fraction in the bleb fluid of secondary burns was toxic to animals, especially if it was not collected at once but after forty-eight hours.

In 1940 Wolff, Elkinton and Rhoads<sup>8</sup> noted changes in hepatic function and glucose tolerance in burned patients in whom shock had been prevented by prompt treatment with plasma. Unfortunately, their patients were treated locally with tanning agents which were later shown to be capable of producing hepatic injury in animals and in human beings.<sup>9</sup>

The experiments of Netsky and Leiter, in 1943,<sup>10</sup> in which an increase in capillary permeability for horse protein occurred in the dog ten minutes after the burn, are of especial interest. They showed not only an increased rate of appearance of the horse protein in the lymph from the burned area but also an increase in the lymph from the unburned area. This seemed difficult to explain, unless an injurious substance was circulating in the blood, a substance essential for normal capillary permeability was withdrawn from the blood or a change in capillary permeability was brought about by nerve control. It was not thought that there was a widespread anoxia at the time the change was first observed.

In the experiments reported here the transfusion of postburn blood did not increase the mortality as compared with that of untreated controls. It did, however, result in a significantly higher mortality than was observed in the animals receiving equal amounts of normal blood. This could be interpreted as indicating the presence of small amounts

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6. Underhill, F. P.; Fisk, M. E., and Kapsinow, R.: The Extent of Edema Fluid Formation Induced by a Superficial Burn, *Am. J. Physiol.* **95**:325, 1930. Underhill, F. P., and Fisk, M. E.: The Composition of Edema Fluid Resulting from a Superficial Burn, *ibid.* **95**:330, 1930. Underhill, F. P.; Fisk, M. E., and Kapsinow, R.: The Relationship of the Blood Chlorides to the Chlorides of Edema Fluid Produced by a Superficial Burn, *ibid.* **95**:334, 1930.

7. Wilson, W. C.; Jeffrey, J. S.; Roxburgh, A. N., and Stewart, C. P.: Toxin Formation in Burned Tissues, *Brit. J. Surg.* **24**:601, 1937.

8. Wolff, W. A.; Elkinton, T. R., and Rhoads, J. E.: Liver Damage and Dextrose Tolerance in Severe Burns, *Ann. Surg.* **112**:159, 1940.

9. Saltonstall, H.; Walker, J.; Rhoads, J. E., and Lee, W. E.: The Influence of Local Treatment of Burns on Liver Function, *Ann. Surg.* **121**:201, 1945.

10. Netsky, M. G., and Leiter, S. S.: Capillary Permeability to Horse Proteins in Burn-Shock, *Am. J. Physiol.* **140**:1, 1943.

of an injurious factor, which counteracted the beneficial effects of the transfusion, or possibly as indicating deficiency of the properties which made the normal blood effective.

#### SUMMARY

Rats subjected to a standardized scald burn were infused with postburn whole blood and normal whole blood. The survival rates of these animals were compared with those of simultaneous untreated controls. The group infused with the postburn blood showed a survival rate similar to that of the untreated group. The animals infused with the normal blood showed a significantly higher survival rate than either of the other two groups. Hematocrit data were obtained from all groups. These give no indication that increased mortality is a direct result of increased hemoconcentration. Suspensions of postburn and normal cells in isotonic solution of sodium chloride were tested. Both promoted increased survival in the test animals when compared with untreated animals; however, the difference between them was not statistically significant. The plasma potassium levels were slightly higher in the postburn blood than in the normal blood. Hemoglobinemia was found to increase from an average value of 75.0 mg. per hundred cubic centimeters in the normal plasma to an average value of 407.0 mg. per hundred cubic centimeters in the postburn plasma.

#### CONCLUSION

Blood from burned rats was ineffective in treatment of rats subjected to a standardized thermal burn resulting in a 44 per cent mortality rate in the untreated controls.

The difference between the mortality rate resulting after transfusion with blood from burned rats (44 per cent) and the mortality rate resulting after transfusion with normal blood (0 per cent) is statistically significant.

Dr. J. E. Rhoads and Dr. Harry M. Vars gave helpful suggestions and criticisms during the course of experimentation and preparation of the manuscript.

## BURN SHOCK

Its Treatment with Continuous Hypodermoclysis of Isotonic Solution of Sodium Chloride Into the Burned Areas; Clinical Studies in Two Cases

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IN A PREVIOUS paper,<sup>1</sup> one of us (J. K. B.) reported the results of experimental studies on burn shock when treated with isotonic solution of sodium chloride injected by hypodermoclysis into the burned area. These studies revealed the following significant facts: 1. There is a loss of water and electrolytes, chiefly salt, followed by plasma proteins into the burned area. 2. This loss continues until pressure in the tissue spaces equals the hydrostatic pressure within the capillaries. Then reabsorption begins but in the reverse manner. That is, colloids are returned first by the lymphatic vessels, which behave as a semipermeable membrane. Then crystalloids are absorbed by the capillaries. 3. The loss of plasma occurs earlier in the more severely (third degree) than in the less severely burned animals. 4. Treatment by hypodermoclysis of isotonic solution of sodium chloride into the burned area seems to decrease the amount of water and plasma lost, and it facilitates the absorption of both. 5. It is thus an autotransfusion of lost colloids and crystalloids and, in addition, is a method for supplying quickly the great demand for salt by injured tissues. 6. It makes possible the dilution and excretion of hypothetical toxins, helps control body temperature and prevents pulmonary edema and anuria. 7. Human skin is not as loosely attached to the subcutaneous tissue as is that of the dog, and therefore multiple injections would be necessary, but much less solution would be needed to produce an intercellular hydrostatic pressure above that of effective capillary pressure.

Recently this method of treatment was used in 2 patients who were burned so extensively that their conditions seemed hopeless. Their burns were due to an explosion of a large tank filled with steaming hot sodium hydroxide. The solution was so strong that practically all the clothes worn by the men fell off their bodies in shreds.

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1. Berman, J. K.; Peterson, L. and Butler, J.: The Treatment of Burn Shock with Continuous Hypodermoclysis of Physiological Saline Solution into the Burned Area, Surg., Gynec. & Obst. **78**:337-345 (April) 1944.

One plasma transfusion (500 cc.) was given to each of the men. Transfusions of whole blood were used at strategic intervals. Although 1 patient (J. E. M.) died after forty days, the other (M. H. P.) survived and is well. In both cases burn shock was controlled or prevented almost entirely by continuous hypodermoclysis of isotonic solution of sodium chloride.

#### REPORT OF CASES

CASE 1.—J. E. M., a 41 year old white man was admitted to the Methodist Hospital at Indianapolis at 5 p. m. on Feb. 16, 1946. About thirty minutes before admission he was burned by hot sodium hydroxide, the result of an explosion of a large tank containing the solution. The burns proved to be second and third degree and involved about 72 per cent of the body surface. The extent of the burned area was estimated by the Berkow<sup>2</sup> and Lund-Browder<sup>3</sup> methods, and the burns were distributed as follows: head, 3 per cent; neck, 1 per cent; anterior part of the trunk, 0 per cent; posterior part of the trunk, 13 per cent; buttocks, 5 per cent; genitalia, 1 per cent; upper part of the arms, 6 per cent; forearms, 6 per cent; hands, 4.5 per cent; thighs, 17 per cent; legs, 13 per cent, and feet, 3 per cent. The total equals 72.5 per cent (fig. 1).

The patient did not appear to be in shock. He was alert and apprehensive and complained of severe pain and coldness. His pulse rate was 130, regular and weak; the respiratory rate was 30, and respirations were shallow, with some dyspnea and an expiratory grunt. Oral temperature was 99 F. The blood pressure was not obtained because both arms and legs were burned. Moist rales could be heard anteriorly in the lower fields of both lungs.

Prior to admission the man was given  $\frac{1}{4}$  grain (0.016 Gm.) of morphine sulfate subcutaneously and 500 cc. of citrated plasma intravenously. Laboratory studies on admission gave the following results: hematocrit reading, 56.5 volumes per cent; plasma protein content, 7.2 Gm.; hemoglobin content, 18 Gm.; erythrocyte count, 5,500,000, and leukocyte count, 27,500, with 95 per cent polymorphonuclears; urinalysis showed specific gravity of 1.038; the albumin content was 2 Gm. per hundred cubic centimeters and sugar content 1.8 Gm. per hundred cubic centimeters.<sup>4</sup>

Treatment.—The patient was given  $\frac{1}{4}$  grain (0.016 Gm.) of morphine sulfate intravenously. Sterile, dry gauze dressings were loosely applied to the extremities,

2. Berkow, S. G.: Method of Estimating Extensiveness of Lesions (Burns and Scalds) Based on Surface Area Proportions, *Arch. Surg.* 8:138-148 (Jan., pt. 1) 1924.

3. Lund, C. C., and Browder, N. C.: The Estimation of Areas of Burns, *Surg., Gynec. & Obst.* 79:352-358 (Oct.) 1944.

4. Laboratory methods: Hematocrit and plasma protein levels were determined by the copper sulfate method for measuring specific gravities (Phillip-Van Slyke and associates); albumin-globulin contents by Kingsley's method for use in Howe's micro-Kjeldahl test; the urine albumin content (quantitative) by Purdy's method; blood sugar levels by the Folin-Wu method; urine sugar (quantitative) by Gerrard-Allen's method; nonprotein nitrogen levels by the Folin-Wu method; carbon dioxide-combining power by Van Slyke's method; blood chloride contents by the "Whitehorn" modification of Volhard's method, and blood calcium levels by Clark-Colly's modification of the Kramer-Tisdall method.

without any attempts to cleanse or antiseptize the wounds. A large 4 ply sterile gauze pad was placed on the bed for the patient to be on, and a cradle was used to keep the sheets and blankets off the burns. No heat was employed externally.

Isotonic solution of sodium chloride was injected by hypodermoclysis into the burned areas by continuous drip. This was accomplished by use of ordinary 1,000 cc. flasks of sterile isotonic solution of sodium chloride equipped with Y tubes and 20 gage, 4 inch (10 cm.) needles. The needles were moved to various parts of the body, all burned areas being kept distended. The infusions were used continuously for ninety-six hours in the amount of 3,000 to 4,000 cc. in twenty-

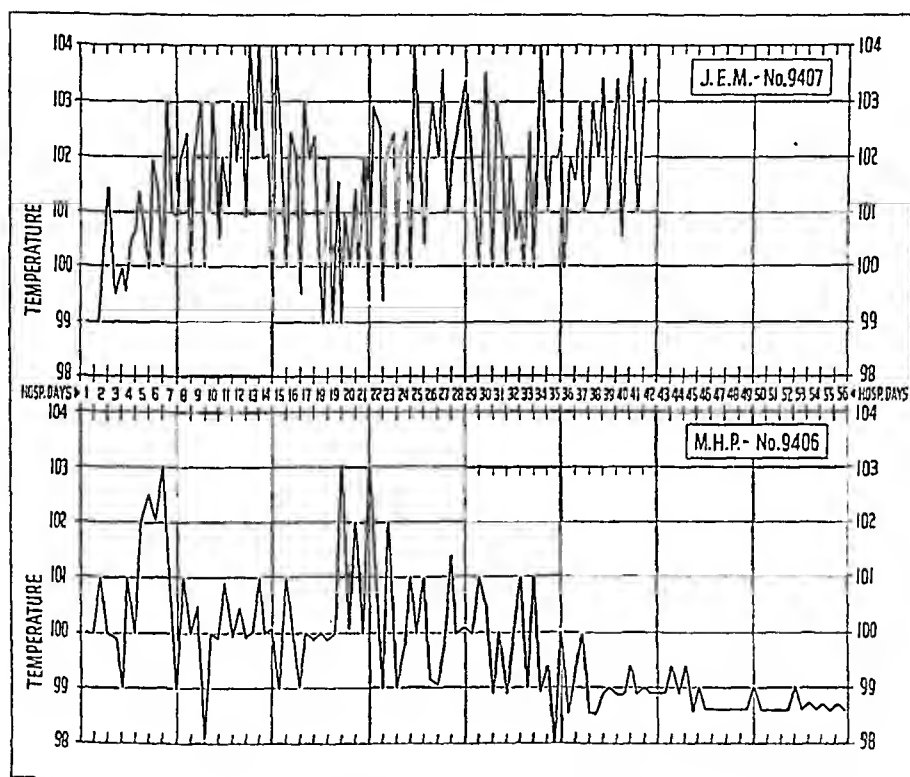


Fig. 1.—The oral temperature (Fahrenheit). Note that J. E. M. had a remittent fever, with temperature up to 104 F. for seventeen days. At this time his temperature tended toward the intermittent type, and its peaks were up to 103 F. Note that at this time the leukocyte count was 15,000, with 84 per cent polymorphonuclears; the fluid intake, 3.5 liters; the urinary output, 2 liters, with specific gravity of 1.015 and no blood in the urine; hemoglobin content, 12.3 Gm.; red blood cells, 4,000,000; hematocrit reading, 45 volumes per cent, and plasma protein level, 4.2 Gm. After this apparent improvement, the patient became worse and the temperature again reached 104 F. and did not at any time fall below 100 F., despite cold sponges on the face, neck and chest carried out by continuous nursing care.

M. H. P. also had a turning point, which occurred on the nineteenth day, with temperature up to 103 F.; leukocyte count, 10,000, with 88 per cent polymorphonuclears; fluid intake, 4.5 liters; urinary output, 4 liters, with specific gravity of 1.012 and no blood in the urine; hemoglobin content, 12.3 Gm.; red blood cells, 4,000,000; hematocrit reading, 41 volumes per cent, and plasma protein content, 4.6 Gm. The patient was in a coma.

four hours. In addition, enteric-coated, 5 grain (0.32 Gm.) sodium chloride tablets were given by mouth; these produced nausea and vomiting, and the administration of them was discontinued after the first day. Penicillin, 30,000 units, was injected intramuscularly every three hours. Tetanus antitoxin, 1,500 units, was given subcutaneously.

A bland, high protein diet was ordered. This included beef broth, beef, cottage cheese, gelatin, milk, buttermilk, custard, bread, potatoes, macaroni and cheese and other foods requested by the patient. Water, tea and sweetened drinks were given as desired, the total calories being about 5,000. Morphine,  $\frac{1}{4}$  grain (0.016 Gm.) was used to relieve pain. Enemas of isotonic solution of sodium chloride were given as needed. A cannula was inserted into the right antecubital vein, and 500 cc. of citrated whole blood was given each day for the first three days.

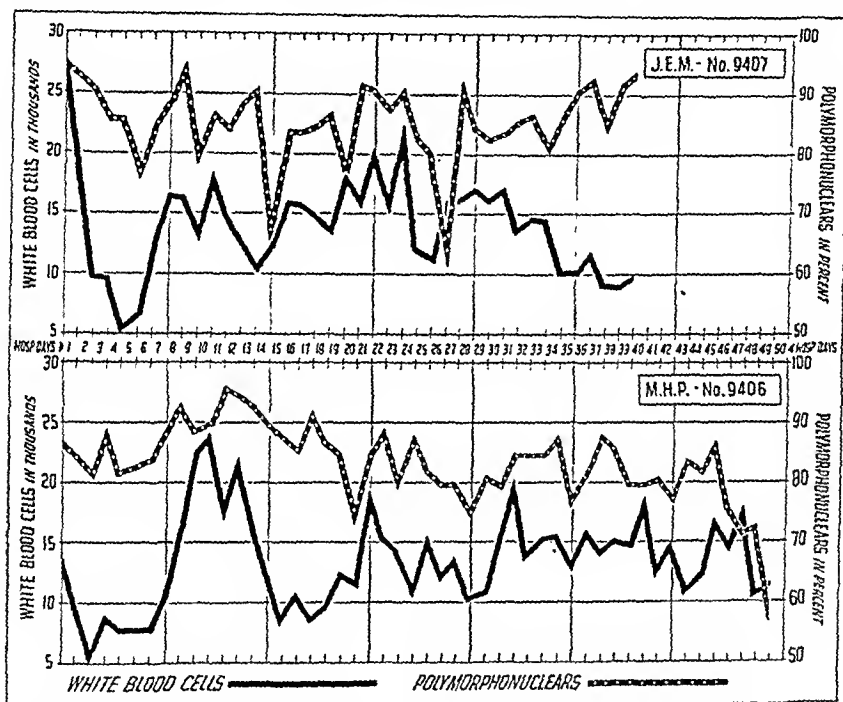


Fig. 2.—Leukocyte and differential counts. Note the initial rise in total count, its precipitous fall by the fourth day (toxic inhibition of bone marrow), then its irregular rise and its falling before death (J. E. M.) and before recovery (M. H. P.) to subnormal and normal levels respectively. The per cent of polymorphonuclears generally followed the total count, except toward the end (J. E. M.), when it rose as the total count fell.

On the third day, almost the entire subcutaneous space of the body, particularly the trunk, was greatly distended with fluid. There was no evidence of pulmonary or other complications, and the patient's clinical appearance was good. Laboratory studies at this time showed hematocrit reading, 51 volumes per cent; plasma protein content, 3.91 Gm. per hundred cubic centimeters, with albumin-globulin ratio of 1:1; hemoglobin content, 17.5 Gm.; red blood cell count, 5,350,000, and white blood cell count, 9,800, with polymorphonuclears 86 per cent.

On the seventh day all areas were covered with dressings of isotonic solution of sodium chloride and penicillin solution, 200 units per cubic centimeter, except

the fingers and toes, which were separated by petrolatum gauze. The temperature had been of the remittent type, but now the peaks reached 104 F. (fig. 1). Penicillin was increased to 50,000 units every three hours. The patient was delirious at intervals. At other times he spoke of his impending death with much anxiety. His reasoning was clear, and his predictions were based on what he had read about extensive burns.

The seventeenth day brought a picture of great emaciation and toxicity. The patient looked septic, with drawn, thin, pale face, sunken eyes and dry mouth. He was apprehensive and irritable. The unburned skin was hot and dry. His temperature reached 103 F.; the respiratory and pulse rates were fast. The

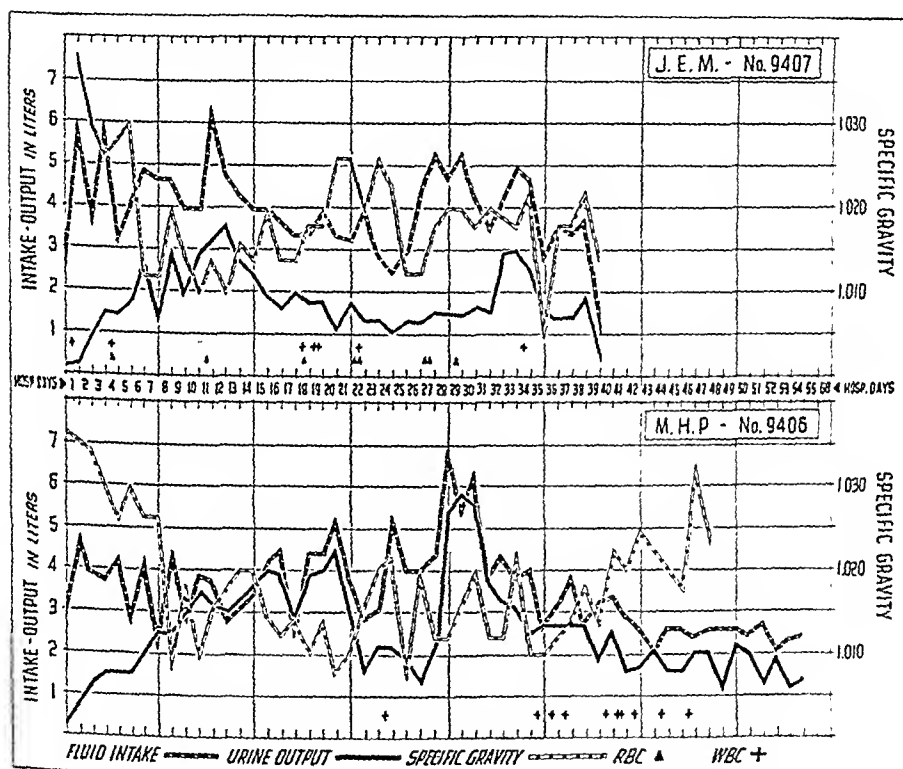


Fig. 3.—Fluid intake by all routes, urinary output, specific gravity and red and white blood corpuscles in the urine. Note the initial anuria, with high specific gravity and blood cell counts despite large intake of fluid. As urinary output increases, specific gravity falls; blood cells are not found. The great variation in specific gravity indicates good renal function but is also dependent on fluid intake and fluid demand. The skin, lungs and gastrointestinal tract take the available interstitial water first (Davis, H. A.: *Proc. Soc. Exper. Biol. & Med.* 43:354, 1940). The kidneys work with whatever is left over. If the temperature is normal, the skin moist and the amount of urine ample, with the specific gravity not too high, there is enough water and the tubules are conserving a normal amount of water. If, in addition, the sensorium is normal and there is no edema, there is not an overhydration. Since renal function is dependent on osmotic as well as hydrostatic pressure, determination of plasma protein content, with albumin-globulin ratio, is helpful as a guide to treatment. The hematocrit reading, red blood cell count and hemoglobin content are guides in the avoidance of anemia or stagnant anoxia, which may also affect urinary excretion. Note the low urinary output of J. E. M., especially after the seventeenth day, except for four days between the thirty-first and thirty-fifth days.



patient was placed in an oxygen tent. Cold sponges of the face and anterior portion of the trunk were carried out at frequent intervals. The burned areas of the lower part of the legs and feet were treated with packs of 0.5 per cent chloramine-T because they were still infected.

The delirium became worse. He had frequent, involuntary, yellow, semiliquid stools as he lay motionless on his back, refusing all food and water and stating repeatedly that he was going to die. Isotonic solution of sodium chloride was given by hypodermoclysis and, in addition, 1,000 cc. of citrated whole blood intravenously. The burned areas looked good. The necrotic skin had been loosened day by day, and the large areas on the back were now covered with healthy granulations or were entirely healed. There was no visible pus except

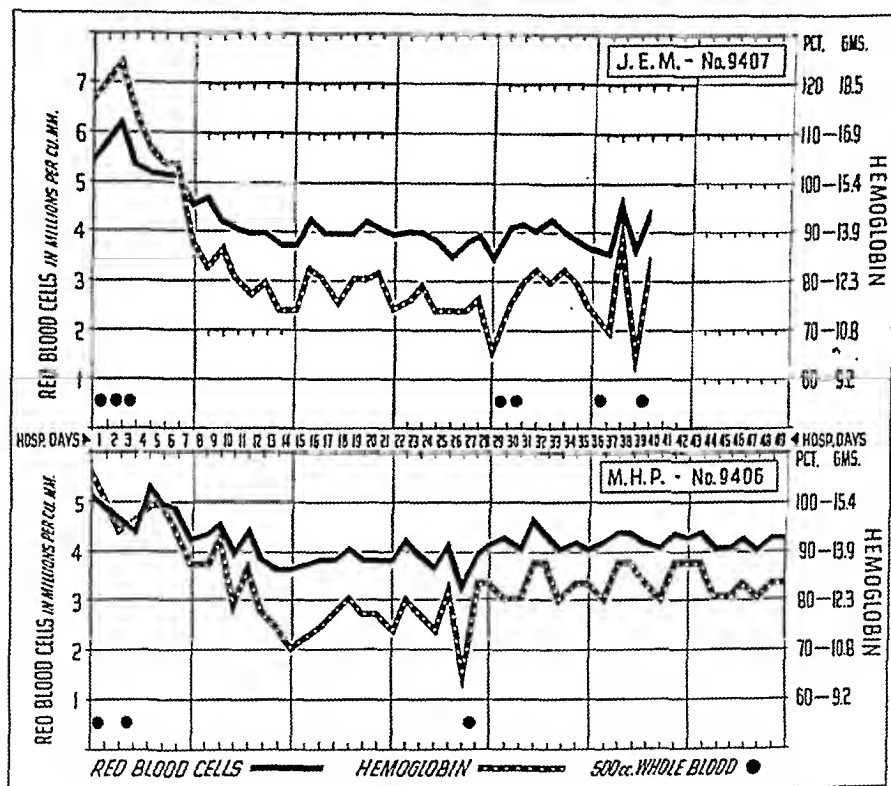


Fig. 4.—Red blood cell count and hemoglobin content are high during the first week because of loss of plasma and water into the burned areas. A more rapid return to normal limits is effected with hypodermoclysis of isotonic solution of sodium chloride and transfusions of whole blood. Patients receiving no specific treatment are also gradually relieved from hemoconcentration by spontaneous hemodilution. J. E. M. had a much higher count (7,200,000) and hemoglobin content (17 Gm., or 112 per cent) than M. H. P.

on some areas of third degree burns of the lower part of the legs and feet. Laboratory studies on the eighteenth day showed: nonprotein nitrogen level, 28 mg. per hundred cubic centimeters; carbon dioxide-combining power, 59.7 volumes per cent; plasma protein content, 4.65 Gm., with 1 Gm. albumin and 3.65 Gm. globulin, per hundred cubic centimeters, and hematocrit reading, 43.5 volumes per cent; leukocytes numbered 16,350, with 83 per cent polymorphonuclears (figs. 2, 3, 4 and 5). Because of low serum albumin content and hematocrit reading, additional

500 cc. units of whole blood and plasma were given on the thirty-fifth and thirty-eighth days. At this time the carbon dioxide-combining power was 102 volumes per cent; erythrocytes, 4,500,000; hemoglobin content, 12.5 Gm.; hematocrit reading, 42 volumes per cent; plasma protein content, 4.4 Gm., with 2 Gm. of albumin, and nonprotein nitrogen level, 27 mg. A persistent, copious diarrhea was present, and the patient had almost continuous, irritating stools. Sulfadiazine, 2.0 Gm., was given every four hours at this time and the buttocks covered with petrolatum gauze. The wounds were clean. The entire back, which was covered with second degree burns, had healed. The thighs were healing rapidly, as were the arms and legs. The face and neck had healed entirely. Urinary output was 1,500 cc. with an intake of 3,500 cc. The urine was acid in spite of a carbon dioxide-

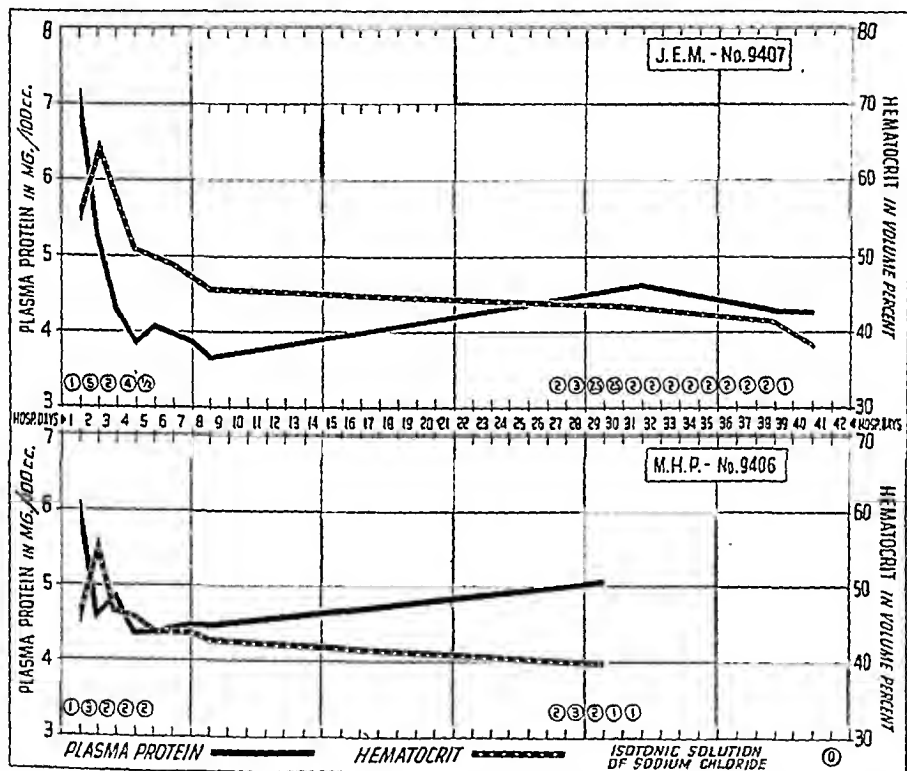


Fig. 5.—Hematocrit reading and plasma protein levels. There is great hemoconcentration during the first forty-eight to seventy-two hours after severe burns. This is due principally to the loss of water and, to a lesser extent, the loss of plasma. Here the plasma protein (chiefly albumin) contents fall rapidly as the hematocrit reading rises. This is quickly controlled with isotonic solution of sodium chloride given in hypodermoclysis into the burned area, which tends to restrict the loss of colloids and crystalloids and augments their reabsorption. Note the fall in hematocrit reading and rise in plasma protein contents as treatment progresses. J. E. M. has more hemoconcentration and slower rise in protein levels than M. H. P.

combining power of 114 volumes per cent. On the thirty-ninth day the patient appeared moribund. Nonprotein nitrogen was 26 mg. The urine was strongly alkaline in reaction. There were muscular twitchings and, later, clonic convulsions. Respirations became labored, and cyanosis was present; the patient became comatose and died on March 28, forty days after admission.

*Postmortem Examination.*—The significant findings, as described by Dr. H. M. Banks, pathologist, were as follows: The peritoneal cavity contained about 100 cc. of clear, light, yellow fluid; an equal amount of the same type of fluid was present in each side of the chest, and about 35 cc. was found in the pericardium. The cardiac muscle was edematous, with small, scattered accumulations of lymphocytes. There was no pulmonary edema. The spleen was large, weighing 240 Gm. It was engorged with blood. The liver showed extensive fatty infiltration and degeneration. Large areas show total destruction of the parenchymal cells of the liver. The kidneys were swollen, and all their blood vessels were dilated and filled with red blood cells. The tubules showed extensive degeneration and in some areas destruction of the lining cells. The tubules contained refractile droplets as seen in nephrosis. Glomeruli and Bowman's capsule showed little deviation from normal; however, the former were dilated and filled with red blood cells. The cerebrum was edematous. In some areas this was extreme. Here the blood

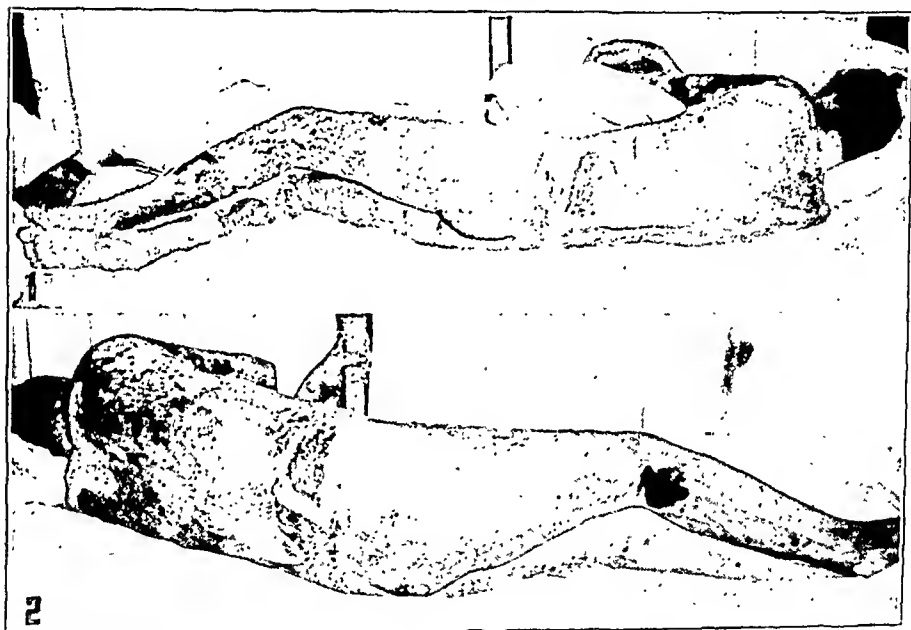


Fig. 6.—A, J. E. M. on the eighth day. B, M. H. P. on the eighth day.

vessels had shriveled and retracted, and surrounding them there were small areas of advanced autolysis. Ganglion cells were pyknotic and degenerated in such areas. The cerebellum showed practically the same picture as the cerebrum. The adrenals contained areas of fatty degeneration and hemorrhagic extravasation, chiefly in the medullary zone.

*Pathologic Diagnosis.*—The pathologic diagnosis was (1) edema of cardiac muscle and acute myocarditis; (2) acute peribronchiolar pneumonia, hemorrhagic phase; (3) fatty infiltration of the liver and toxic atrophy of the liver; (4) acute nephrosis and chronic passive congestion of the kidneys, and (5) massive autolysis of the cerebrum, with cerebral edema.

CASE 2.—M. H. P., a 43 year old white man, was admitted to the hospital at the same time as J. E. M. He had been burned by the same explosion, over about 71 per cent of his body surface. Although most of the burns were second

degree, the areas involved by third degree were more extensive than in the previous case. The Berkov and Lund-Browder tables being used, the extent and distribution of the burns were estimated to be as follows: head, 2 per cent; neck, 1 per cent; anterior portion of the trunk, 0 per cent; posterior portion of the trunk, 13 per cent; buttocks, 5 per cent; genitalia, 0 per cent; upper part of the arms, 5 per cent; forearms, 6 per cent; hands, 4.5 per cent; thighs, 19 per cent; legs, 13 per cent, and feet, 2.5 per cent. The total equaled 71 per cent of the body surface (fig. 2).

The patient had received exactly the same treatment as J. E. M. prior to his admission to the hospital. He was in severe pain and apprehensive and complained of being cold. His pulse rate was 150 per minute and was thready; the respiratory rate was 30 and the temperature 100 F. orally. The blood pressure was not taken because the cuff could not be applied without great discomfort. Mr. P. was given exactly the same treatment as Mr. M. Laboratory studies showed a hematocrit level of 47 volumes per cent; plasma protein content, 6.15 Gm.; hemoglobin content, 16.5 Gm.; red blood cells, 5,190,000, and white blood cells, 14,300 per cubic millimeter, with 87 per cent polymorphonuclears. Urinalysis showed specific gravity, 1.036; albumin content, 1 Gm. per hundred cubic centimeters, and sugar, 3.8 Gm. per hundred cubic centimeters, with a trace of acetone.

*Treatment.*—Isotonic solution of sodium chloride was administered by hypodermoclysis into the burned areas, as previously described. Three to 4 liters in twenty-four hours was given. Sodium chloride tablets taken by mouth caused nausea and vomiting, and the administration of them was discontinued. Thirty thousand units of penicillin were given intramuscularly every three hours. Diet and liquids allowed were the same as for J. E. M. Five hundred cubic centimeters of citrated whole blood was given through an ankle vein on the first day, and the injection was repeated on the third day. Laboratory studies, on the third day, revealed a hematocrit reading of 46 volumes per cent; plasma protein content, 4.39 Gm., and albumin-globulin ratio, 1.4:1.0 (figs. 1 to 5). At this time the subcutaneous space of the entire body was greatly distended with isotonic solution of sodium chloride. Its administration was discontinued on the fourth day.

The burns were treated with packs of isotonic solution of sodium chloride, and sloughs were removed carefully each day. Petrolatum gauze was wrapped around the fingers and toes. Butacaine sulfate and merthiolate ointment was used in the eyes for chemical conjunctivitis.

On the eleventh day penicillin was increased to 40,000 units every three hours intramuscularly, because of the persistent fever, which was accompanied with wild delirium. Leukocytes numbered 18,500 per cubic millimeter, with 96 per cent polymorphonuclears. By the sixteenth day the temperature was 99.4 F. orally, and the wounds were clean.

On the nineteenth day the fever returned, and the temperature reached 103 F. orally. The patient was confused. Hallucinations and illusions were interspersed with periods of stupor. The latter were followed by generalized muscular twitchings, which at times became gross clonic and tonic convulsions. There was some cyanosis, and the patient refused food and water. Reflexes were hyperactive. The diagnoses of possible tetany or tetanus or diabetes were considered. Laboratory tests gave the following results: blood chloride content, 561 mg.; blood calcium content, 8.9 Gm.; nonprotein nitrogen level, 26.5 mg.; carbon dioxide-combining power, 30 volumes per cent on March 12, 1946, 47.5 volumes per cent on March 13 and 50.4 volumes per cent on March 16; blood sugar content on March 12 was 204 mg., twelve hours later 135 mg. and on March 13, 190 mg.

At this time hypodermoclysis of isotonic solution of sodium chloride, which had been discontinued on the fourth day, was again started. About 2 liters a day

were absorbed. In addition, the patient was given 500 cc. of whole blood, placed in an oxygen tent and given sodium amytal, 3 grains (0.19 Gm.) intramuscularly as required to control convulsions. Practically all second degree burns had healed. Some third degree burns had healthy granulations and were ready for split thickness grafts. All open wounds were covered with packs of isotonic solution of sodium chloride. Isotonic solution of sodium chloride was injected beneath the burns, sufficient to cause slight weeping. This was repeated once a day. Sloughs were removed each day as they became loose. The injection of isotonic solution of sodium chloride facilitated this greatly.

On the twenty-ninth day the hypodermoclysis of isotonic solution of sodium chloride was again discontinued. The patient was greatly improved. He was given a high protein regular diet and a preparation of vitamin B complex (Becotin<sup>5</sup>) containing thiamine hydrochloride, 3 mg.; riboflavin, 6 mg.; pyridoxine hydrochloride, 1.5 mg.; nicotinamide, 30 mg.; pantothenic acid, 10 mg., and desiccated fraction of liver-stomach concentrate with yeast extract, 0.6 Gm.

The patient was allowed to sit on the side of the bed thirty-seven days after admittance. Skin had to be grafted on some areas, but most wounds healed without excessive scarring, owing to the fact that they were second degree burns.

The patient was released from the hospital fifty-five days after admittance. He was last seen on July 23, 1946, at which time he had entirely recovered.

#### COMMENT

The treatment of burn shock with hypodermoclysis of isotonic solution of sodium chloride is simple and effective. It is also useful in neutralizing or diluting hypothetic toxins, as illustrated in the case of M. H. P., whose burn toxemia was adequately controlled by this method, and at least partially neutralized in the case of J. E. M. While 2 cases are insufficient to prove any concept, these observations, coupled with the experimental work referred to, form a basis for further study. The patient who died had an alkalosis which may have been due to an excess of sodium. Parenteral administration of fluids (except whole blood) was withheld for forty-eight hours prior to his death; yet the urine remained acid until eight hours ante mortem. The patient took small amounts of water by mouth during this time. Since free fluid was present in the serous cavities, it may seem that too much isotonic solution of sodium chloride was given. A careful review of the case does not bear this out. This is interesting because it illustrates the fact that the fluid will be absorbed from the tissue spaces for osmotic reasons even though the heart is unable to properly propel the absorbed fluid. However, this need not prevent the use of adequate amounts of isotonic solution of sodium chloride by hypodermoclysis, because if the hydrostatic pressure due to cardiac inadequacy exceeds osmotic pressure the sodium chloride given subcutaneously will remain in situ.

A note of warning concerning excessive administration of sodium and fluid should be sounded. Even though the fluid is given subcutaneously or by mouth, we believe that in the late stages of burn

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5. Becotin is manufactured by Eli Lilly and Company.

toxemia slight underhydration is safer than overhydration and acidosis is more easily controlled than alkalosis. Our patient (J. E. M.) probably died from toxemia, which was never completely controlled, although practically the same situation was present in the man who recovered (M. H. P.).

At autopsy J. E. M. showed extensive necrosis of the liver and cerebral autolysis. Morphologically, renal changes, such as pigmented casts in the tubules and tubular necrosis, are present in hemolytic reactions to blood transfusion and in burns. Pigment casts were not found in this case, perhaps because the urine was alkaline most of the time.

Burn shock and early burn toxemia may be prevented or adequately controlled by the method outlined. The deciding factor seems to be persistent toxemia, which is probably due to a combination of causes such as dehydration, oligoplasma, stagnant anoxemia, infection and the absorption of toxins directly from the burned area and secondarily from damage to the liver and kidneys. Most of these integrants may now be successfully dealt with. Infection is still a problem in extensive burns. The best local treatment is to protect the wounds from trauma and let them severely alone, except as already described.<sup>6</sup> Should infection occur, antibiotics (penicillin locally and systemically) and chemotherapeutic agents (sulfadiazine, orally or parenterally) should be used judiciously.

The control of persistent toxemia is a real challenge in burns involving more than 50 per cent of the body surface. Although it may be partially neutralized by sodium, there are still other factors which must be more clearly understood before prolonged burn toxemia can be successfully controlled.

One last problem should be mentioned concerning skin grafting. Had M. H. P. been the victim of third degree burns entirely, then the only available donor site would have been the anterior part of the chest and upper part of the abdomen. Taking skin from this unburned area is hazardous, as it may swing the balance of effects from a 70 per cent burn to one of 100 per cent. Therefore, only small areas could be grafted at any one time.

#### CONCLUSIONS

1. The use of isotonic solution of sodium chloride by continuous hypodermoclysis into the burned area is strongly recommended in extensive burns for the treatment of burn shock and toxemia.

2. Isotonic solution of sodium chloride by hypodermoclysis is useful during the granulation stage of burn wounds to increase resistance to infection and to stimulate healthy granulation tissue.

6. Berman, J. K.; Houser, A. D., and Kurtz, W. A.: Wound Immunity. *Surg., Gynec. & Obst.* 77:205-208 (Aug.) 1943.

## CYSTS OF THE DUODENUM

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CYSTS of the duodenum are rarely reported in the literature. Twelve cases of enterogenous cysts of the duodenum have been described since the initial case of Sanger and Klopp,<sup>1</sup> in 1880. A cyst of the ampulla of Vater, described by Brooks and Weinstein,<sup>2</sup> appears to be one of the mucosa covering the ampulla of Vater, and yet it was both lined and covered with normal duodenal mucous membrane so that, as the authors described, this cyst was a congenital anomaly of the duodenal wall. Microscopic study of this cyst was not reported. These authors were unable to find a similar condition in the literature except the anomalous duodenal pouch presented by Grant,<sup>3</sup> a pouch of mucosa which "hung within the lumen of the gut like a hollow polypus whose mouth was directed towards the pylorus." This pouch showed a reduplication of the entire mucous membrane of the intestine and had the pouch been closed off at its superior margin it would have presented a structure similar to that in the case of Brooks and Weinstein. No Brunner's glands were seen in this pouch. Vogt,<sup>4</sup> in 1925, described a benign perforating duodenal cyst which arose as a retroperitoneal cyst derived from the vestigial remains of the wolffian body and which invaded the duodenum. Vogt considered this to be an endodermal parallel of a teratoma or dermoid cyst, but it represents secondary involvement of the duodenum by extension only. Cysts of Brunner's glands themselves have not been reported as a cause for surgical intervention in duodenal obstruction.

This report is made because of the rarity of duodenal cysts and the occurrence of two of different types within six weeks in the experience of the authors, the two presenting somewhat identical clinical syndromes of intermittent duodenal obstruction, with similar roentgenologic and gross pathologic findings but necessitating different surgical procedures.

From the Gastric Service of the Memorial Hospital for the Treatment of Cancer and Allied Diseases.

1. Cited by Gardner and Hart.<sup>18</sup>

2. Brooks, B. B., and Weinstein, A.: Cyst of Ampulla of Vater, *Ann. Surg.* **117**:728-734, 1943.

3. Grant, J. C.: Anomalous Duodenal Pouch, *Brit. J. Surg.* **23**:233-234, 1935.

4. Vogt, M. E.: Benign Perforating Duodenal Cyst Arising from the Vestigial Remains of the Wolffian Body, *Am. J. Obst. & Gynec.* **10**:798-802, 1925

*Collected Cases of Enterogenous Cysts of the Duodenum*

| <i>Case</i> | <i>Year</i> | <i>Operator</i>      | <i>Sex</i> | <i>Age</i> | <i>Symptoms</i>   | <i>Physical Examination</i>   | <i>Prognostic</i><br><i>Dilemma</i>                 | <i>Location</i>   | <i>Size</i>                       | <i>Operation</i>   | <i>Result</i>                            |
|-------------|-------------|----------------------|------------|------------|---|---|---|---|-----------------------------------|--|--|
| 1           | 1880*       | Silvers and Klopp    | (?)        | Newborn    | .....   | .....   | .....   | Three cysts of intestine, 1 arising from accessory bile duct and 1 from accessory liver; large pedunculated cyst arising in third portion of duodenum | "Size of a walnut"                | .....  | Infant died during delivery              |
| 2           | 1881*       | Roth                 | M          | Newborn    | .....   | Abdomen tremendously distended  | .....   | Large pedunculated cyst arising in third portion of duodenum  | .....                             | Also had enterogenous cyst of mediastinal esophagus                    | Infant died a few minutes after delivery |
| 3           | 1910        | Mayer                | F          | 3 wk.      | Persistent vomiting beginning at 2 wk.  | .....   | Pyloric stenosis                                    | Cyst extended from pylorus to ampulla of Vater  | "Size of a hen's egg"             | No operation   | .....                                    |
| 4           | 1922        | Waugh                | F          | 10 days    | Regurgitation and vomiting  | Thin tumor in right side of abdomen   | "Tumor of right hypochondrium                       | Large cyst presented on outer side of ascending colon   | "Size of a taugotino"             | I. Cyst evacuated and packed; II. Marsupialization                     | Died 6 days after second operation       |
| 5           | 1927        | Maddox               | (?)        | 3 mo.      | Projectile vomiting beginning at 6 wk.  | Hard mass in right upper quadrant   | Pyloric obstruction (?)                             | Second portion of duodenum  | "Size of a goose egg"             | Posterior gastro-enterostomy attempted                                 | Died on first hospital day               |
| 6           | 1930        | Smith                | F          | 2 wk.      | Vomiting  | Abdominal distention; palpable tumor  | Congenital pyloric stenosis                         | Cyst of anterior wall of first portion  | "Size of a hantam's egg"          | Section of wall removed; pylorus dilated; exterior drainage            | Died on seventh post-operative day       |
| 7           | 1931        | Gardner and Hart     | F          | 15 yr.     | Vomiting with attacks of pain   | Mass in right upper quadrant  | Choledochus cyst                                    | First and second portions of the duodenum   | Approximately 10 cm. (?)          | Enterocystostomy   | Complete recovery                        |
| 8           | 1933        | Tachman              | F          | 4 mo.      | Vomiting  | Freely movable mass   | Cyst of abdomen                                     | First portion of duodenum; intramural   | 8 by 11 cm.; contents 550 cc.     | Partial marsupialization   | Died 4 hr. postoperatively               |
| 9           | 1933        | Hasman               | F          | 4 wk.      | Projectile vomiting   | Freely movable mass   | Pyloric stenosis                                    | Anterior part of first portion  | 2 to 3 cm. long; contents 15 cc.  | I. Evacuation; II. Gastro-enterostomy                                  | Complete recovery                        |
| 10          | 1940*       | Ladd and Gross       | F          | 5 wk.      | Regurgitation and vomiting  | Freely movable soft cystic mass above the navel                                     | Onental cyst or enteric cyst                        | Along mesenteric border of first portion of duodenum  | 4.5 by 3.5 cm.                    | Resection of cyst and first portion of duodenum with gastroenterostomy | Prolonged recovery                       |
| 11          | 1940        | Gillespie and Rogers | M          | 4 1/2 yr.  | Faundula, malaise, abdominal pain, anorexia and abdominal mass of 1 week's duration | Moderate degree of tenderness; freely movable globular mass in right upper quadrant | .....   | Behind second portion of duodenum, intramural   | 12 cm. in diameter; 350 cc. fluid | Cyst freed; aspirated and discolored mass excised; duodenum closed     | Uneventful recovery                      |
| 12          | 1941        | Ovrigus              | M          | 2 mo.      | Projectile vomiting   | Cystic, mobile tumor of right upper quadrant  | Renal neoplasm                                      | Pylorus and first portion of duodenum stretched over cyst   | 3 in. (7.5 cm.) in diameter       | Resection with gastroduodenostomy                                      | Uneventful recovery                      |
| 13          | 1945        | Pack and Booher      | M          | 17 yr.     | Intermittent attacks of nausea and vomiting and pyralism                            | Fixed mass in right epigastrium   | Adenoma (?); myoma (?); cyst of Brunner's gland (?) | Posterior medial wall; first portion extending into second portion  | 2 cm. in diameter; 8 cc. contents | Emulectomy   | Complete recovery                        |

\* Date reported; other dates indicate year of operation.



## AGE AND SEX DISTRIBUTION

There are no data available concerning the age and sex distribution of cysts of Brunner's glands. In Feyrter's <sup>5</sup> case, presenting cystic degeneration of an adenoma, the condition occurred in a man "more than 54 years" of age. Our patient was a man of 52. Of the enterogenous cysts reported, two have occurred in males and eight in females and in 2 cases there was no record as to sex. The ages varied from newborn to 15 years, our 17 year old youth being the third male and the oldest patient recorded.

## INCIDENCE

Robertson <sup>6</sup> found 2 instances of cystic dilatation of Brunner's glands in gross examination of 15,000 cases, with microscopic examination in more than 1,000 of them. He cited Rutishauser's presentation of 6 of his own and made a comprehensive review of carcinoma of the duodenum, in which he found 1 case presenting three nodules in the upper portion of the duodenum, which proved to be cysts filled with mucin. Feyrter studied the duodenums of 2,800 patients, in 3 of whom glandular adenomas were found, one of these presenting cystic dilatations containing degenerated cells and masses of mucin. Pack and McNeer <sup>7</sup> collected 16 cases of Brunnerian adenoma from the literature, but none presented evidence of cystic degeneration or retention. Rabinovitch and Pines <sup>8</sup> have found an asymptomatic inclusion cyst of Brunner's gland in the tail of the pancreas in a 42 year old man at necropsy. The cyst wall was made up of a delicate layer of connective tissue lined on the inside by a layer of tall columnar epithelium with a subjacent layer of mucinous glands, which they interpreted as Brunner's glands. Such ectopic origin can be explained on the basis of fetal inclusion, the detachment and independent development of intestinal tissue in some part of the embryo in which it should not occur.

Ackermann <sup>9</sup> reported the incidence of diverticula of the duodenum discovered at autopsy as varying from 3.3 per cent of 1,367 of Lensmayer's cases to 15.5 per cent of Schuppel's cases and an incidence on roentgenologic examination varying from 0.016 per cent of 72,715 examinations by Rankin and Martin to 5.19 per cent of Cryderman's examinations in 770 cases. He found an even higher incidence by making plaster molds of the duodenums of cadavers and found eleven

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5. Feyrter, cited by Robertson.<sup>6</sup>

6. Robertson, H. E.: The Pathology of Brunner's Glands, *Arch. Path.* **31**: 112-130 (Jan.) 1941.

7. Pack, G. T., and McNeer, G.: Unpublished data.

8. Rabinovitch, J., and Pines, B.: Cysts of the Pancreas, *Arch. Surg.* **45**: 727-746 (Nov.) 1942.

9. Ackermann, W.: Diverticula and Variations of the Duodenum, *Ann. Surg.* **117**:403-413, 1943.

diverticula in 50 consecutive cases, an incidence of 22 per cent. Yet he made no mention in this series of finding the embryologic counterpart or sequela, that is, an enteric cyst. Pachman,<sup>10</sup> reviewing 36 cases of enterocysts, found 28 cases of cysts in the terminal ileum or ileocecal area as compared with 8 in the duodenum. Ladd and Gross,<sup>11</sup> in 1940, reported 18 patients with cystic lesions situated along various parts of the intestinal canal, which they called "duplications of the alimentary tract," but only one cyst was in the duodenum.

#### ETIOLOGY AND PATHOLOGY

Robertson's discussion of degeneration and infiltration of Brunner's glands and the resultant pathologic changes is comprehensive:

The outstanding characteristic of the glands is their comparative freedom from influences which ordinarily affect secreting tissues. General toxemias, starvation states and dietary deficiencies apparently leave them unscathed. The cells at times have an almost clear cytoplasmic content, staining only faintly or not at all with ordinary dyes or even with specific mucin stains, and the ducts are free from stainable substances. This condition has been pointed out as evidence of increased function, but I have observed it in the region of duodenal ulcers and other inflammatory processes in the mucosa of the duodenum. Occasionally there is stasis of secretion, with dilated ducts and acini. In some cases this is evidently because of obstruction to the ducts; it has been observed in the region of invading or metastatic tumor nodules and on the margins of chronic or healed ulcers. Such a condition may lead to cyst formation, in which acini or even an entire lobule may be dilated and contain a mass of cell detritus mixed with varying amounts of mucin. . . . More rarely occur large cysts reaching several millimeters in diameter and producing easily observable nodules in the duodenal wall. . . . These cysts are lined with low cuboid cells, and the lumens are largely free from stainable substances.

Hartz and van der Sar,<sup>12</sup> contrary to Robertson, concluded that in the presence of inflammatory conditions the epithelium of Brunner's glands reacts in the same way as glandular epithelium in other parts of the body. With this viewpoint it is even more surprising that evidence of hypersecretion and subsequent retention is not observed more frequently, when one considers the many and variable stimuli the duodenal mucosa receives.

Information as to the position in the duodenum and the size of cysts of Brunner's gland is lacking. Robertson stated that the size varies from the dilatation of a lobule to cysts several millimeters in diameter. Feyrter's adenomas ranged from the size of a pea to that

10. Pachman, D. J.: Enterogenous Intramural Cysts of the Intestines, *Am. J. Dis. Child.* **58**:485-505 (Sept.) 1939.

11. Ladd, W. E., and Gross, R. E.: Surgical Treatment of Duplications of the Alimentary Tract, *Surg., Gynec. & Obst.* **70**:295-307, 1940.

12. Hartz, P. H., and van der Sar, A.: Proliferative Activity in Brunner's Glands, *Am. J. Path.* **20**:931-943, 1944.

of a hazelnut, but the size of the cyst is not given. Our patient presented a cyst 1.5 by 2 cm. occurring on the anterior wall of the duodenum.

There are several theories concerning the causation of enterogenous cysts. Lewis and Thyng,<sup>13</sup> in a review of the occurrence of intestinal diverticula in embryos of the pig, the rabbit and man, concluded that "knoblike" intestinal diverticula occur regularly in these embryos, and their presence was noted in the cat and the sheep. The authors were of the opinion that these "knoblike" diverticula were the probable source of an occasional accessory pancreas and that they usually degenerated, sometimes forming detached cysts and nodules. It was felt that these structures might give rise to pathologic diverticula. Ewing<sup>14</sup> concurred that they might arise from misplaced portions of the intestine and stated that Beneke had designated cysts of this origin as "entodermoid."

It does not seem likely that enteric cysts arising as far cephalad as the duodenum should arise from Meckel's diverticulum or the vitello-mesenteric duct, which is a possible source of origin for those of the ileomesenteric area. Orgias<sup>15</sup> concluded that the cyst in his case "is a developmental cyst of the duodenum and has developed as a diverticulum of the first part of the duodenum." Evans,<sup>16</sup> in reviewing both enterogenous cysts and diverticula of the intestine, stated: "There can be no doubt that cysts whose walls reproduce completely or incompletely the structure of gut, whether discovered in the wall of the gut, attached to the gut, or even more or less remote from the gut, must have been derived from gut. They are developmental cysts."

Hughes-Jones<sup>17</sup> proposed a theory of epithelial sequestration as a possible origin of enterogenous cysts. He made serial sections of a number of human embryos and in 2 found evidence of epithelial sequestration. In 1 a small cyst was lined by epithelium resembling that of the adjacent bowel. Hughes-Jones felt that these islets were separated before the circular musculature was formed and that after they were formed the isolated epithelium gained its muscle coat by a condensation of the undifferentiated mesenchyme surrounding the intestine.

If these "knoblike" diverticula or misplaced or displaced enteric anlagen are the source of origin for both cysts and diverticula, it is

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13. Lewis, F. W., and Thyng, L.: The Regular Occurrence of Intestinal Diverticula in Embryos of the Pig, Rabbit and Man, *Am. J. Anat.* **7**:505-519, 1907.

14. Ewing, J.: *Neoplastic Diseases*, ed. 4, Philadelphia, W. B. Saunders Company, 1940, pp. 1062-1063.

15. Orgias, R.: Enterogenous Cyst, *Brit. J. Surg.* **31**:90-93, 1943.

16. Evans, A.: Enterogenous Cysts and Diverticula, *Brit. J. Surg.* **17**:34-83, 1929.

17. Hughes-Jones, W. E. A.: Enterogenous Cysts, *Brit. J. Surg.* **22**:134-141, 1934.

surprising that primary diverticula of the duodenum are so frequent and cysts so uncommon if they are in reality different phases of the same process.

Enterogenous cysts may occur anywhere in the wall of the bowel or in the mesentery and are classified as submucosal, intramuscular, subperitoneal and intramesenteric. They have occurred most frequently in the second portion of the duodenum but have extended up to the pylorus and have arisen behind the first portion. The size has varied from the size of a walnut to cysts containing 500 cc. of fluid. The average size has been approximately 6 to 7 cm. in diameter.

By definition, the walls of these cysts correspond to the structure of the intestinal canal. They present well defined muscular coats and glandular linings, and, although intracystic pressure may cause atrophy and flattening of the glands, the glands of Brunner are apparent.

#### SYMPTOMS AND FINDINGS

Except for the patients in the first 2 reported cases, the cysts in whom were discovered at autopsy, all patients with enterogenous cysts have presented signs and symptoms of duodenal obstruction, so that a diagnosis of pyloric stenosis was entertained in cases of infants. Persistent vomiting or regurgitation has been the predominant symptom, twice occurring with pain. In 9 of the 12 cases of enterogenous cysts previously reported a tumor had been palpable. In only 1 of our cases, that of the enteric cyst, was a mass palpable. The most important diagnostic signs noted by Gardner and Hart<sup>18</sup> were palpable tumor and signs of duodenal obstruction. Pachman's analysis of symptoms and findings in his report of 8 cases of intramural cysts is most complete, and any one having unusual interest in this subject is referred to his comprehensive review of enterogenous cysts. Ladd and Gross observed that most cysts of the duodenum, jejunum and ileum brought early signs of intestinal obstruction, characterized by colic-like pain, vomiting, increased peristalsis and, finally, signs relating to dehydration. Hemorrhage due to interference with intestinal blood supply has not occurred in the duodenal lesions, unless the unexplained hematemesis occurring at the age of 6 months in the patient of Gardner and Hart was due to the cyst which was operated on fourteen years later, though there had been no continuity of symptoms. In only the case of Gillespie and Rogers<sup>19</sup> was there evidence of biliary obstruction. Since

18. Gardner, C. E., Jr., and Hart, D.: Enterogenous Cysts of Duodenum: Report of a Case and Review of the Literature, *J. A. M. A.* **104**:1809-1812 (May 18) 1935.

19. Gillespie, J. B., and Rogers, J. C.: Enterogenous Cysts of the Duodenum. *Arch. Pediat.* **57**:652-658, 1940.

only two of the previously reported cysts were in patients over 4 months of age, it appears that these lesions, if they occur in the duodenum, produce symptoms early and that the cysts have little opportunity to attain great size.

Cysts of Brunner's glands are usually asymptomatic.

#### ROENTGENOLOGIC DIAGNOSIS

In the case of Ladd and Gross there was sufficient compression of the first and second portions of the duodenum to give evidence of partial obstruction. In the case of Pachman there were no findings on gastrointestinal examination to suggest obstruction, though the infant presented peristaltic waves and was vomiting at the time. The case of Gardner and Hart presented no apparent anomaly on gastrointestinal roentgenologic study. Our roentgenologic findings have been similar and definite. Both patients have presented a round central filling defect of the second portion of the duodenum, but there has been nothing characteristic to differentiate it from papilloma or polypoid benign tumor of the wall.

#### TREATMENT

Four methods of surgical approach are possible: (1) duodenal resection with the adjacent cyst, (2) enucleation or excision, (3) simple evacuation and (4) marsupialization.

Of the 12 cases of enterogenous cysts reported to date, there have been 5 cases of recovery following surgical removal. The first reported cyst, of Sanger and Klopp, in 1880, was discovered at autopsy in an infant who died during a difficult delivery. The patient of Roth,<sup>15</sup> in 1881, died a few minutes after delivery, and in the case of Meyer,<sup>18</sup> reported in 1919, a diagnosis of pyloric stenosis was made, but the patient died without surgical intervention. Waugh,<sup>20</sup> in 1923, apparently was the first to operate on an enterogenous cyst of the duodenum. His patient was a 19 day old girl and he found a retroperitoneal cyst which was adherent to the posterior wall of the duodenum. He packed the cavity of the cyst with gauze, but six weeks after the removal of the gauze it refilled. Six weeks later the child was operated on again, the cyst wall being sutured to the aponeurosis of the abdominal wall, but the child died of pneumonia six days after the second procedure. Posterior gastroenterostomy was attempted for Maddox'<sup>21</sup> patient, but the condition of the child made it impossible to complete the operation.

20. Waugh, O. S.: Congenital Cyst of the Duodenum, *Surg., Gynec. & Obst.* 37:785-787, 1923.

21. Maddox, K.: Cyst of the Duodenum Simulating Pyloric Obstruction, *M. J. Australia* 1:900, 1927.

The child died the day of the operation. Smith,<sup>22</sup> in 1930, operating on a 2 week old infant with a cyst of the anterior wall of the duodenum, drained it externally. The child died one week postoperatively, the cyst having regressed greatly in size. The first successful operation was that of Gardner and Hart, in 1929, who treated a 15 year old girl by anastomosing the cyst to the intestinal tract. In Basman's<sup>23</sup> case, reported in 1938, of a 4 week old child presenting signs of pyloric stenosis, evacuation of the cyst alone was done because of the poor condition of the infant, but in seven days the tumor was again palpable and the abdomen was reopened, showing that the cyst had refilled. An attempt was made to enucleate the cyst, but when the operator failed to find a line of cleavage a gastroenterostomy was performed.

In Pachman's case, after 550 cc. of greenish black thin fluid had been aspirated, a small portion of cyst wall was removed for biopsy and a small catheter was inserted and secured to the peritoneal opening to effect partial marsupialization. The infant died four hours after operation. Ladd and Gross resected the first portion of the duodenum and performed a posterior gastrojejunostomy. Gillespie and Rogers aspirated 350 cc. of the contained fluid from their patient and then excised the collapsed discoid sac and inverted the duodenal wall. This presented a technical difficulty insofar as the medial wall of the excision was adjacent to the common bile duct, but when the duct was probed before the abdomen was closed it showed no obstruction. In the last case reported, Orgias attempted to dissect the cyst off the posterior portion of the pylorus and the first portion of the duodenum but, finding it impossible, resected the involved portion of the stomach and duodenum with subsequent end to end anastomosis, with an uneventful recovery.

In our case an intramural enterogenous cyst was enucleated, as was attempted in the cases of Basman and Orgias, and though a good line of cleavage was not possible it was shelled out by both sharp and blunt dissection and the muscular and mucosal layers closed separately.

Ladd and Gross stated that the treatment of enterogenous cysts consists in complete excision, with removal of the attached portion of the alimentary tract. They recommend this because their experience has shown that the masses cannot be enucleated without danger of perforating the viscus or leaving it in an ischemic state. We concur with this even after successful enucleation in our case. The feeling that our second case presented similar findings to our first case, in

22. Smith, R. E.: A Case of Enterocystoma of the Duodenum Simulating Congenital Pyloric Stenosis, *Guy's Hosp. Rep.* 80:463-465, 1930.

23. Basman, J.: Enterogenous Cyst of the Duodenum Simulating Pyloric Stenosis: Report of a Case in an Infant with Recovery Following Gastroenterostomy, *J. Pediat.* 12:363-366, 1938.

which the mass enucleated so easily, caused us to pursue the procedure once it was undertaken, even though difficulty became apparent. Examination of the wall revealed no perforation of the muscularis and good color of the entire duodenal wall, so that the procedure was concluded at this stage. However, the fear of jeopardizing the viability of bowel wall by enucleation may be more theoretic than actual insofar as Miller<sup>24</sup> recorded 10 cases of enucleation in the ileocecal region, without a death.

Of the 6 survivors in the 13 collected cases, 2 have had resection of the adjacent duodenum, gastrointestinal continuity being reestablished by gastrojejunostomy and gastroduodenostomy once each. One patient had a gastrojejunostomy after drainage of the cyst, and 1 had only an enterocystostomy, a remarkably successful form of uncomplicated evacuation. Two instances of local excision with successful results are recorded. This represents an operative mortality of 45.4 per cent and a case mortality rate of 53.8 per cent.

Enucleation of the cysts of Brunner's glands is not attended with the difficulties inherent in management of the enterogenous cyst. Simple enucleation is sufficient for this problem, which presents grossly similar findings.

#### REPORT OF CASES

CASE 1.—E. A., a 52 year old white man, was first seen on July 24, 1945, complaining of loss of weight, anorexia and fatigue of three months' duration. He had occasional abdominal cramps, which he attributed to constipation. He had never observed melena or clay-colored stools.

General physical examination revealed a normally proportioned man, weighing 150 pounds (68 Kg.), who presented no evidence of jaundice but appeared anemic. He had no cervical adenopathy, and the thyroid gland was not enlarged. The heart, lungs and blood pressure were normal. Examination of the abdomen revealed no tenderness in the epigastrium or over the duodenum. No masses were palpable, and the liver and spleen could not be palpated. Results of urinalysis were entirely normal, and the red blood cell count was 3,670,000, hemoglobin 79 per cent, or 11.5 Gm. per hundred cubic centimeters by the Sahli method, and the white blood cell count 12,000, with polymorphonuclears 65 per cent, lymphocytes 32 per cent, monocytes 2 per cent and eosinophils 1 per cent.

The submitted report of roentgenographic examination by Dr. Maurice Rona showed a normal chest except for a large ossified primary focus of primary tuberculosis infection in the middle lobe of the right lung, which was deemed entirely inactive. A series of roentgenograms of the gastrointestinal region, taken on July 10, was reported as follows: The stomach is medium in size and normal in position, shape, outline, tone and peristaltic contraction, filling smoothly in all its parts, without evidence of organic changes. The pyloric valve shows a tendency toward spasm. The bulb is small to medium in size and somewhat flattened in shape but without evidence of organic defects. The second portion of the duodenum fills out normally, but at the region of the papilla of Vater an oval-

24. Miller, R. T.: Enterogenous Mesenteric Cysts, *Bull. Johns Hopkins Hosp.* 24:316-322, 1913.

shaped filling defect 1.5 cm. in width is constantly present and suggests a tumefaction arising from the papilla. The loop of the duodenum is apparently widened, but no evidence of pressure and no change in the mucosal outline are seen. The jejunum and ileum show some scattering of barium but no gross abnormalities. The motility of the stomach and of the small intestines is normal.

*Résumé.*—The findings in the gastrointestinal tract may be regarded as normal except for the tumefaction in the descending duodenum. The nature of the tumefaction cannot be determined from the roentgenograms alone.

Cholecystograms revealed a normally functioning and noncalculous gallbladder.

The presumptive diagnosis was papillary tumor of the duodenum. Laparotomy and removal of the duodenal polyp by the transduodenal route were recommended.

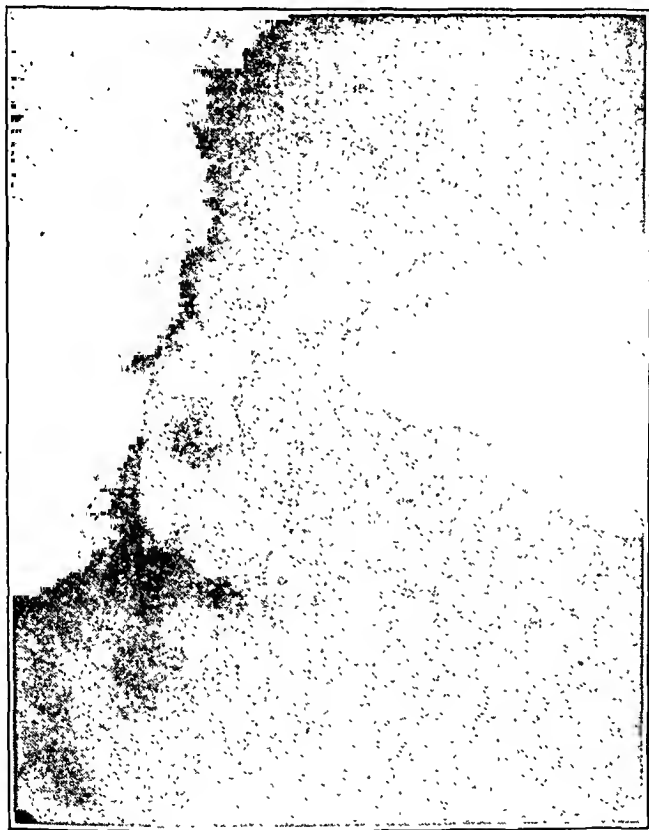


Fig. 1 (case 1).—In this roentgenogram the second portion of the duodenum fills out normally, but at the region of the papilla of Vater an oval-shaped filling defect 1.5 cm. in width is present. It suggests a tumefaction arising from the papilla of Vater.

The patient was admitted to the Memorial Hospital for the Treatment of Cancer and Allied Diseases on July 30, 1945, and laparotomy was performed the following day. A right paramedian celiotomy was done, and, on palpation of the second portion of the duodenum, a smooth cystic mass measuring 1.5 by 2 cm. was palpated on the anterior wall of the second portion, extending to the left wall. A transverse incision was made over the mass in the second portion of the duodenum, and the cyst was seen to be covered entirely by mucosa and seemed



to be within the mucosa itself. It was well encapsulated and contained whitish mucoid fluid. The cyst was opened and evacuated and a careful dissection carried out, the capsule being removed. The duodenal mucosa was repaired, and at completion of this stage the gallbladder was compressed and the flow of bile indicated free evacuation of the gallbladder. The duodenal wall was then closed in three layers and the incision closed in layers, with drainage to the site of duodenal closure.

The postoperative course was complicated by localized peritonitis, which responded to penicillin therapy. The patient was entirely asymptomatic by the fourth postoperative day and was discharged on the fifteenth postoperative day.



Fig. 2 (case 1).—Photomicrograph showing that beneath a moderately attenuated duodenal mucosa are multiple cystic spaces which arise in glands or ducts of Brunner's glands. In many of these foci the lining epithelium is of characteristic type, but in other areas it is cuboidal.

*Pathologic Examination.*—The specimen consists of a small sac; one area is covered by mucosa and the remaining two thirds by roughened, frayed, muscular tissue. The wall is approximately 0.4 mm. thick.

*Microscopic Examination.*—Beneath a slightly to moderately attenuated duodenal mucosa are multiple cystic spaces, which obviously have their origin in glands or ducts of Brunner's glands. In many of these foci the lining epithelium is of characteristic type, but in some areas the lining cells become cuboidal and somewhat more opaque. Here and there are scattered and inconspicuous uniradicular papillary excrescences, but in general the cystic spaces have a single epithelial lining. The largest of the cystic spaces is about 1.5 mm., but larger

spaces may have been disrupted prior to receipt of the specimen. Sections do not include muscularis.

*Diagnosis.*—The diagnosis was multiple cysts of Brunner's glands.

CASE 2.—I. B., a 17 year old white student, was referred from the medical clinic of Dr. Lloyd F. Craver at the Memorial Hospital for the Treatment of Cancer and Allied Diseases on June 22, 1945. He complained of vomiting early in the morning occurring about twice monthly since he was 12 years old. The usual sequence of these periodic bouts of vomiting was ptyalism, early morning nausea and epigastric pain which would be constant for periods of two to three minutes and then subside, to return again in about fifteen minutes. The whole attack would last about one hour, but the sense of nausea would usually persist through the day. These attacks were associated with nervous tension and were not associated with food intake. About a year after the symptoms appeared his family doctor was consulted, and a series of roentgenograms of the gastrointestinal tract was made and the patient told that there was "a scratch in the wall of the stomach." He was placed on a diet, which he followed with little constancy, and the vomiting spells continued to occur once or twice a month. Approximately eight months before the patient had come to the Memorial Hospital for the Treatment of Cancer and Allied Diseases, another doctor had taken a series of roentgenograms of the gastrointestinal region and had told the patient that he had a benign tumor. The patient was again placed on a diet, and the vomiting spells ceased but nausea continued in the early morning and, occasionally, epigastric pain. His appetite was poor, but he had daily bowel movements and had no other gastrointestinal complaints. The month before admission his local draft board had classified him as 4F because roentgenographic studies revealed "some pathology in the stomach." The only significant item in his past history was an uncomplicated bilateral mastoidectomy at the age of 4. He used both alcohol and tobacco occasionally, and his family history presented no history of carcinoma, tuberculosis or diabetes.

Physical examination revealed a slightly undernourished and sallow boy, weighing 123 pounds (55.8 Kg.). The lungs, heart and blood pressure were apparently normal. There was tenderness in the right paraumbilical region, and a small fixed mass could be palpated just to the right of the spinal column, slightly above the umbilicus. The liver, spleen and kidneys were not palpable, and no abdominal, iliac or inguinal nodes could be felt. The laboratory studies revealed hemoglobin of 95 per cent, 4,400,000 red blood cells per cubic centimeter and a white blood cell count of 9,300, with 59 per cent polymorphonuclear filamented forms, 6 monocytes and 35 per cent lymphocytes. Results of urinalysis were normal except for an occasional red blood cell.

Roentgenologic studies of the gastrointestinal tract on July 6, 1945 were reported by Dr. Ruth Snyder, as follows: On fluoroscopy, the esophagus canalized normally. The stomach showed no intrinsic disease; there was good peristalsis and emptying. The duodenal cap showed a deformity, with a concavity on the side of the greater curvature. This was constant and apparently due to a tumor within its walls in this location. The roentgenograms showed a deformity of the duodenal cap similar to that seen on submitted roentgenograms (dated Feb. 19, 1940 and Dec. 2, 1944), and the appearance suggests a fairly large tumor of the wall of the cap on the side of its greater curvature. This may be due to a polyp or myoma or similar process. It is not obstructing, and the stomach was almost emptied at one hour.

The patient was then admitted to the hospital, on July 7, 1945, and additional spot roentgenograms of the duodenal cap showed no change in the defect in the midportion and distal portion of the cap. Gastric analysis showed no blood or bile, with 100 degrees of free hydrochloric acid and 106 degrees of total acidity and, on repetition, 47 degrees of free hydrochloric acid and 53 degrees of total acidity. Stool specimens showed no occult blood.

The presumptive diagnosis was benign tumor of the duodenum, either myoma or adenoma, though one member of the staff was influenced by the preceding case and made a diagnosis of duodenal cyst.



Fig. 3 (case 2).—The roentgenogram of the duodenal cap shows a deformity, with a concavity on the greater curvature side. The appearance suggests a fairly large tumor of the wall of the cap on its greater curvature side.

On September 10 exploratory laparotomy was done through a midline incision in the upper part of the abdomen. On palpation of the first portion of the duodenum and just beyond the pylorus and extending into the second portion of the duodenum, a firm, tense mass was palpated. On palpation it could be separated from the head of the pancreas. The anterior wall of the duodenum was easily movable over it. Palpation of the liver revealed no cysts, and palpation of the right kidney was noncontributory. The second portion of the duodenum was mobilized by Kocher's maneuver. A longitudinal incision was made in the anterior wall of the duodenum, beginning 2 cm. distal to the pylorus and

extending to the papilla of Vater. This exposed the tumor of the posteromedial wall of the duodenum. The mucosa was freely movable over it. A needle was introduced into the cyst, and 8 cc. of clear slightly mucilaginous fluid was obtained. Incision was then made through the mucosa, and the wall of the cyst was identified. With blunt dissection the wall of the cyst was separated from the mucosa, though the wall of the cyst was ruptured during the procedure. The cystic capsule was removed by a combination of blunt and sharp dissection and the muscular wall sutured with a running suture to control oozing from this area. The mucosa was closed to effect complete hemostasis. The anterior duodenal wall was closed in a transverse direction with a Connell inverting suture and a seromuscular continuous locked suture of silk. An

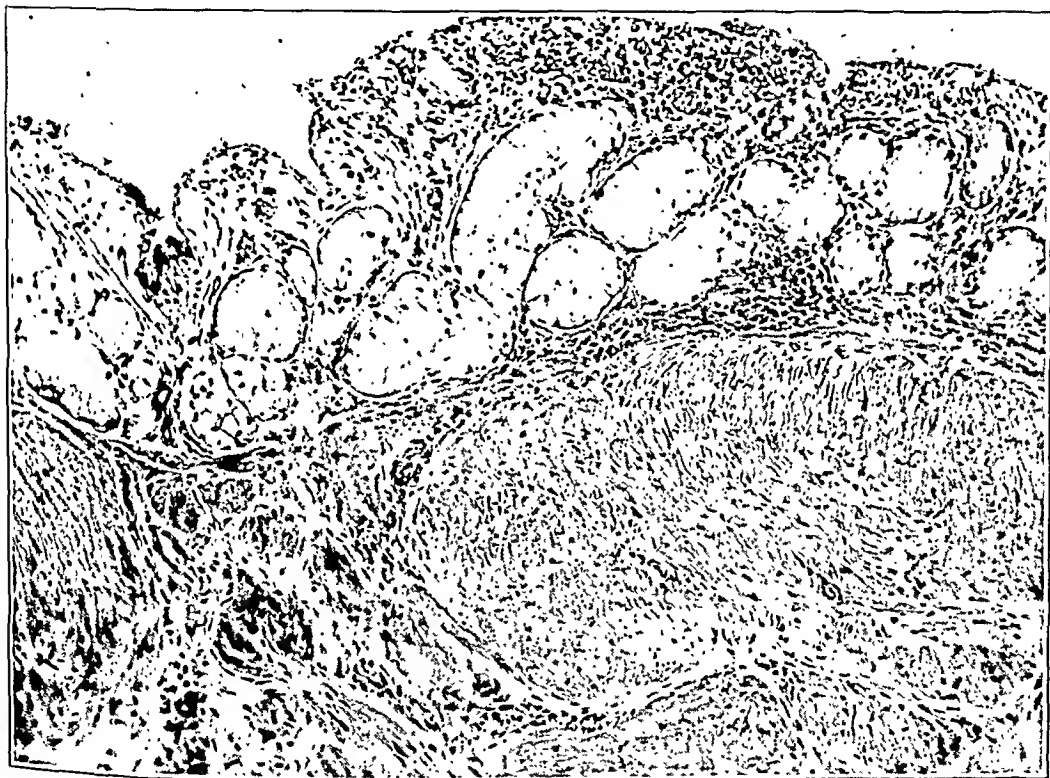


Fig. 4 (case 2).—The photomicrograph presents the internal margin of the cyst wall. The circular and longitudinal muscular coats are about one-fourth to one-third normal thickness. Brunner's glands are reduced in mass and number. There is moderate interstitial fibrosis and round cell infiltrate. The atrophic duodenal mucosa is not included in the section.

indwelling Levine tube was then guided into the third portion of the duodenum. The abdominal wall was closed in layers with silk and reenforced with retention sutures, with one cigaret drain placed over Morrison's pouch.

One transfusion of 500 cc. was given on the third day, though the blood count was essentially unchanged from the first count. The hospital course was uneventful, the drain being completely removed by the fifth day, the last sutures out by the twelfth and the patient home on the twelfth postoperative day. The patient has been seen in the clinic since that time, and for the first six weeks

after leaving the hospital he had occasional periods of nausea in the early morning. A series of roentgenograms of the gastrointestinal region on October 23 showed a postoperative deformity of the duodenal bulb but no obstruction in the first and second portions of the duodenum. Since that time the patient has been asymptomatic and is back to employment in a new field, as a dental technician, free of all symptoms, having gained 3 pounds (1.3 Kg.).

*Pathologic Examination.*—The specimen consists of a small cyst, with a diameter of approximately 2 cm. Part of the wall consists of frayed muscular tissue. The interior of the cyst is smooth and presents no unusual gross characteristics.

*Microscopic Examination.*—There is almost complete atrophy of the duodenal mucosa; there is only a single epithelial layer, which is variously columnar to low cuboidal. The lamina muscularis mucosa is scarcely recognizable, being reduced to a filamentous membrane. The circular and longitudinal muscular coats are about one fourth to one third of the normal thickness. Brunner's glands are greatly reduced in mass and are entirely absent in multiple areas. There is moderate interstitial fibrosis accompanied with a fairly dense round cell infiltrate. This is most prominent in the areas of Brunner's glands but involves the entire muscular wall in some areas.

*Diagnosis.*—The lesion represents a form of congenital cystic dilatation of the duodenum.

#### SUMMARY

1. The problem of duodenal cysts has been reviewed.
2. A case of cystic dilatation of Brunner's glands is recorded, the first necessitating surgical intervention for duodenal obstruction.
3. The thirteenth case of a patient with an enterogenous cyst of the duodenum is recorded, the sixth patient who has survived operation. The operative mortality rate for these collected cases is 45.4 per cent.
4. The surgical management of these cystic lesions has been discussed.
5. Simple enucleation of the cysts, with reconstruction of the wall and transverse closure of a duodenotomy in the longitudinal plane, has relieved the symptoms of obstruction in these 2 patients.
6. Simple enucleation is adequate treatment for cysts of Brunner's glands, but this procedure applied to an enterogenous cyst may be attended with injury to the duodenal wall.

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## PATHOLOGY AND PHYSIOLOGY OF STRUMA OVARII

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**T**HYROID tissue develops fairly frequently in ovarian dermoids (table 1), although it is usually no more than a microscopic portion of the tumor. There is, however, a rare type of ovarian tumor, known as struma ovarii, in which thyroid tissue is a major constituent.<sup>1</sup> Some of these ovarian goiters are obvious teratomas, containing besides thyroid such tissues as skin, teeth, brain and intestinal epithelium. Others consist entirely of thyroid or of thyroid in association with a cystoma:

Boettlin in 1889 was the first to note the presence of thyroid tissue in an ovarian dermoid. Wilms, Merttens and Kroemer published reports

TABLE 1.—Incidence of Thyroid Tissue in Ovarian Teratomas

| Author                        | Teratomas | Thyroid | Per Cent    |
|-------------------------------|-----------|---------|-------------|
| Pick.....                     | 21        | 6       | 28.6        |
| Neumann.....                  | 74        | 5       | 6.7         |
| Rohdenburg.....               | 61        | 9       | 16.4        |
| Mayer.....                    | 131       | 2       | 1.5         |
| Koucky.....                   | 125       | 19      | 14.8        |
| Melgs.....                    | 27        | 2       | 7.4         |
| Spencer.....                  | 66        | 1       | 1.5         |
| Trübedl and De.....           | 31        | 3       | 9.7         |
| Gusberg and Danforth.....     | 297       | 8       | 2.7         |
| Blackwell and associates..... | 100       | 13      | 13.0        |
| Salter.....                   | 37        | 3       | 8.1         |
| Total.....                    | 973       | 71      | Average 7.3 |

of similar cases. Then Gottschalk in 1899 described an ovarian tumor composed entirely of thyroid-like tissue. Thyroid tissue in the midst of a dermoid was not remarkable, but an ovarian tumor composed entirely of thyroid seemed improbable. Gottschalk concluded, despite its structural similarity to thyroid, that the tumor was derived from ovarian follicles. Because one portion had the histologic appearance of a malignant growth, Gottschalk named the tumor "folliculoma malignum."

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1. The term struma ovarii is often loosely applied to any ovarian teratoma containing thyroid tissue; only the tumors in which there has been considerable unilateral development of thyroid tissue should be so designated.

TABLE 2.—*Published Cases of Struma Ovarii*

| Author                               | Year | Case | Age,<br>Yr. | Pathology                                | Comment                                | No. |
|--------------------------------------|------|------|-------------|--|--|-----|
| Adolf.....                           | 1918 | 1    | 51          | Dermoid with thyroid                     | Ascites                                | 1   |
|                                      |      | 2    | 40          | Dermoid with thyroid                     | Dermoid of opposite ovary              | 2   |
| Aisenstadt.....                      | 1913 | 1    | 26          | Dermoid with thyroid                     | Cystic ovary on opposite side          | 3   |
| Anspach.....                         | 1903 | 1    | 36          | Dermoid with thyroid                     | .....                                  | 4   |
| Asekanasy.....                       | 1936 | 1    | 36          | Cystoma with thyroid                     | .....                                  | 5   |
|                                      |      | 2    | 34          | Cystoma with thyroid                     | Goiter present                         | 6   |
|                                      |      | 3    | 32          | Dermoid with thyroid                     | .....                                  | 7   |
| Moraes Barros, de Godoy and Delenclo | 1914 | 1    | 39          | Thyroid                                  | .....                                  | 8   |
| Bauer.....                           | 1914 | 1    | 27          | Cystoma with thyroid                     | .....                                  | 9   |
| Bell.....                            | 1905 | 1    | 32          | Cystoma with thyroid                     | .....                                  | 10  |
|                                      |      | 2    | 52          | Dermoid with thyroid                     | Goiter present                         | 11  |
| Boettlin.....                        | 1899 | 1    | 28          | Dermoid with thyroid                     | .....                                  | 12  |
| Bolt.....                            | 1923 | 1    | 61          | Dermoid with thyroid                     | Ascites                                | 13  |
| Boxer.....                           | 1911 | 1    | 42?         | Thyroid                                  | Ascites                                | 14  |
|                                      |      | 2    | 42?         | Cystoma with thyroid                     | .....                                  | 15  |
|                                      |      | 3    | ?           | Thyroid                                  | Dermoid of opposite ovary              | 16  |
| Brandenburg.....                     | 1936 | 1    | 38          | Dermoid with thyroid                     | Goiter present                         | 17  |
| Brown.....                           | 1942 | 1    | 57          | Thyroid                                  | Ascites                                | 18  |
| Bua.....                             | 1922 | 1    | 24          | Thyroid                                  | Goiter present                         | 19  |
| Büll.....                            | 1919 | 1    | 32          | Cystoma with thyroid                     | .....                                  | 20  |
| Cantor and Kogut.....                | 1936 | 1    | 21          | Thyroid                                  | Coincident pregnancy                   | 21  |
| Castano.....                         | 1939 | 1    | 54          | Dermoid with thyroid                     | Goiter present                         | 22  |
| Oleland.....                         | 1910 | 1    | ?           | Dermoid with thyroid                     | .....                                  | 23  |
| Cohn and Kushner.....                | 1944 | 1    | 52          | Dermoid with thyroid                     | .....                                  | 24  |
| Dingels.....                         | 1912 | 1    | 58          | Cystoma with thyroid                     | Ascites                                | 25  |
| Erland.....                          | 1936 | 1    | 60          | Thyroid                                  | Cranial metastases                     | 26  |
| Einge.....                           | 1940 | 1    | 31          | Dermoid with thyroid                     | .....                                  | 27  |
|                                      |      | 2    | 20          | Cystoma with thyroid                     | Omental implants                       | 28  |
| Eversmann.....                       | 1905 | 1    | 33          | Cystoma with thyroid                     | .....                                  | 29  |
| Fuhmy.....                           | 1936 | 1    | 64          | Cystoma with thyroid                     | Ascites                                | 30  |
| Flebaeh.....                         | 1911 | 1    | 50          | Cystoma with thyroid                     | Cyst of opposite ovary; ascites        | 31  |
| Frank.....                           | 1909 | 1    | 22          | Dermoid with thyroid                     | .....                                  | 32  |
| Frankel und Lederer.....             | 1928 | 1    | 50          | Cystoma with thyroid                     | .....                                  | 33  |
|                                      |      | 2    | 54          | Dermoid with thyroid                     | Ascites                                | 34  |
|                                      |      | 3    | 34          | Dermoid with thyroid                     | .....                                  | 35  |
| Frankl.....                          | 1912 | 1    | 42          | Thyroid                                  | Histologic evidence of malignancy      | 36  |
| Frankl.....                          | 1924 | 1    | 29          | Dermoid with thyroid                     | .....                                  | 37  |
|                                      |      | 2    | 23          | Dermoid with thyroid                     | Cystoma of opposite ovary              | 38  |
| Frankl.....                          | 1931 | 1    | 62          | Thyroid and Brenner tumor                | Granulosa cell tumor of opposite ovary | 39  |
| Frankl.....                          | 1934 | 1    | 30          | Dermoid with thyroid                     | Goiter removed at age 18 yr.           | 40  |
| Funke.....                           | 1900 | 3    | ?           | Dermoid with thyroid                     | .....                                  | 41  |
| Gargano.....                         | 1928 | 1    | 45          | Thyroid with chorion-epithelioma         | Omental implants                       | 42  |
| Gemmell.....                         | 1911 | 1    | ?           | Dermoid with thyroid                     | .....                                  | 43  |
| Giannettaslo.....                    | 1914 | 1    | 32          | Teratoma with thyroid                    | Bilateral tumors; ascites              | 44  |
| Glockner.....                        | 1903 | 1    | 57          | Dermoid with thyroid                     | .....                                  | 45  |
| Gottschalk.....                      | 1899 | 1    | 48          | Thyroid                                  | Ascites                                | 46  |
| Gusberg and Danforth..               | 1944 | 1    | 53          | Dermoid with thyroid                     | Goiter present                         | 47  |
| Haggag.....                          | 1927 | 1    | 57          | Cystoma with thyroid                     | .....                                  | 48  |
| Helmsen.....                         | 1932 | 1    | 74          | Cystoma with thyroid, cartilage and bone | Goiter present                         | 49  |
| Hundley.....                         | 1940 | 1    | 41          | Dermoid with thyroid                     | .....                                  | 50  |

TABLE 2.—*Published Cases of Struma Ovarii—Continued*

| Author                                      | Year | Case | Age,<br>Yr. | Pathology.                      | Comment   | No. |
|---|------|------|-------------|---------------------------------|---|-----|
| Kafka.....                                  | 1921 | 1    | 63          | Dermoid with thyroid            | Ascites   | 51  |
|   |      | 2    | 22          | Dermoid with thyroid            | .....   | 52  |
|   |      | 3    | 60          | Dermoid with thyroid            | .....   | 53  |
| Katsurada.....                              | 1901 | 4    | 48          | Dermoid with thyroid            | .....   | 54  |
| King and Norris.....                        | 1930 | 1    | 45          | Cystoma with thyroid            | .....   | 55  |
|   |      | 2    | 36          | Dermoid with thyroid            | Coincident pregnancy  | 56  |
| Kleine.....                                 | 1934 | 3    | 43          | Dermoid with thyroid            | .....   | 57  |
|   |      | 1    | 39          | Cystoma with thyroid            | .....   | 58  |
|   |      | 2    | 55          | Dermoid with thyroid            | Goiter present  | 59  |
|   |      | 3    | 53          | Cystoma with thyroid            | Ascites   | 60  |
|   |      | 4    | 49          | Teratoma with thyroid           | .....   | 61  |
|   |      | 5    | 38          | Teratoma with thyroid           | Goiter present  | 62  |
| Koerner.....                                | 1925 | 6    | 35          | Teratoma with thyroid           | .....   | 63  |
|   |      | 1    | 26          | Dermoid with thyroid            | .....   | 64  |
| Kovacs.....                                 | 1924 | 1    | 33          | Thyroid                         | Goiter present  | 65  |
| Kretschmar.....                             | 1901 | 1    | 48          | Cystoma with thyroid            | Goiter present;   | 66  |
|   | 1902 |      |             | and bone                        | patient died 2 yr. later of "Rezidiv"; ascites                                |     |
| Kroemer.....                                | 1899 | 10   | ?           | Dermoid with thyroid            | .....   | 67  |
| Lanz.....                                   | 1902 | 1    | 54          | Thyroid                         | Cirrhosis of the liver and ascites present                                    | 68  |
|   |      |      |             |                                 |   |     |
| Leeene.....                                 | 1904 | 1    | 40          | Dermoid with thyroid            | .....   | 69  |
|   |      | 2    | ?           | Dermoid with thyroid            | .....   | 70  |
| Lindquist and Forselius.                    | 1915 | 1    | 52          | Dermoid with thyroid            | .....   | 71  |
| Lochrane.....                               | 1933 | 1    | 43          | Cystoma with thyroid            | .....   | 72  |
| Lyday.....                                  | 1934 | 1    | 19          | Cystoma with thyroid            | .....   | 73  |
| Macleod.....                                | 1932 | 1    | ?           | Dermoid with thyroid            | Dermoid of opposite ovary   | 74  |
|   |      | 2    | ?           | Dermoid with thyroid            | .....   | 75  |
| Manasse.....                                | 1926 | 1    | 53          | Teratoma with thyroid           | Bilateral teratomas with thyroid; papillary tumor of thyroid tissue           | 76  |
|   |      |      |             |                                 |   |     |
| Masson and Mueller.....                     | 1933 | 1    | 49          | Cystoma with thyroid            | Goiter; ascites   | 77  |
|   |      | 2    | 55          | Cystoma with thyroid            | Ascites   | 78  |
|   |      | 3    | 63          | Thyroid with calcification      | .....   | 79  |
|   |      | 4    | 39          | Cystoma with thyroid            | Goiter; ascites   | 80  |
|   |      | 5    | 38          | Thyroid                         | Nodule of thyroid tissue in ovary only 6 mm. in diameter; goiter also present | 81  |
|   |      | 6    | 43          | Cystoma with thyroid            | Goiter present  | 82  |
| Maxwell.....                                | 1911 | 1    | 47          | Cystoma with thyroid            | .....   | 83  |
| Merttens.....                               | 1897 | 1    | 6           | Dermoid with thyroid            | .....   | 84  |
| Meyer.....                                  | 1903 | 1    | 55          | Thyroid with bone               | Ascites   | 85  |
| Moench.....                                 | 1915 | 1    | 44          | Dermoid with thyroid            | Goiter present  | 86  |
|   | 1929 | 2    | 46          | Dermoid with thyroid            | Goiter present; opposite ovary cystic   | 87  |
| Mohr.....                                   | 1912 | 3    | 49          | Dermoid with thyroid            | Thyrototoxicosis?   | 88  |
|   |      | 1    | 62          | Dermoid with thyroid            | Metastasis to liver and diaphragm   | 89  |
| Möller.....                                 | 1915 | 1    | 35          | Dermoid with thyroid            | .....   | 90  |
| Nomigliano.....                             | 1924 | 1    | 34          | Dermoid with thyroid            | .....   | 91  |
| Morgen.....                                 | 1924 | 2    | 55          | Dermoid with thyroid; bilateral | Peritoneal implantations, which underwent spontaneous regression; ascites     | 92  |
|   |      |      |             |                                 |   |     |
| Murray, Dockerty and Pemberton              | 1942 | 1    | 56          | Dermoid with thyroid            | Granulosa cell tumor of opposite ovary  | 93  |
| Neu (same case reported by Sitzler in 1913) | 1911 | 1    | 42          | Thyroid                         | .....   | 94  |



TABLE 2.—Published Cases of Struma Ovarii—Continued

| Author                   | Year          | Case | Age,<br>Yr. | Pathology  | Comment  | No. |
|--------------------------|---------------|------|-------------|--|--|-----|
| Neumann.....             | 1937          | 1    | 28          | Dermoid with thyroid                                       | .....  | 95  |
|                          |               | 2    | 30          | Cystoma with thyroid                                       | Cartilage and bone present                           | 96  |
|                          |               | 3    | 27          | Cystoma with thyroid                                       | Golter present                                       | 97  |
| Nicholson.....           | 1937          | 1    | 69          | Cystoma with thyroid                                       | .....  | 98  |
| Norris.....              | 1909          | 1    | 51          | Dermoid with thyroid                                       | .....  | 99  |
| Outerbridge.....         | 1913          | 1    | 37          | Cystoma with thyroid                                       | Ascites  | 100 |
|                          |               | 2    | 52          | Dermoid with thyroid                                       | .....  | 101 |
| Parodi.....              | 1922          | 1    | 53          | Cystoma with thyroid                                       | Ascites  | 102 |
| Plek.....                | 1902          | 1    | 33          | Dermoid with thyroid                                       | .....  | 103 |
| Piltz.....               | 1910          | 1    | 57          | Dermoid with thyroid                                       | .....  | 104 |
| Plauchu and Gaudon....   | 1923          | 2    | 21          | Dermoid with thyroid                                       | .....  | 105 |
| Plaut.....               | {1931<br>1933 | 1    | 47          | Cystoma with thyroid                                       | Histologically "malignant" areas                     | 106 |
|                          |               | 2    | 35          | Cystoma with thyroid                                       | Cystoma of opposite ovary                            | 107 |
|                          |               | 3    | 55          | Cystoma with thyroid                                       | Ascites  | 108 |
| Polano.....              | 1904          | 1    | 56          | Thyroid  | Ascites  | 109 |
| Poll.....                | 1910          | 1    | 41          | Dermoid with thyroid                                       | .....  | 110 |
| Pollosson and Violet.... | 1905          | 1    | 63          | Dermoid with thyroid                                       | .....  | 111 |
| Proescher and Roddy....  | 1910          | 1    | 36          | Cystoma with thyroid                                       | .....  | 112 |
|                          |               | 2    | 26          | Cystoma with thyroid                                       | Bone also present                                    | 113 |
|                          |               | 3    | 37          | Thyroid  | Metastasis to liver, omentum and mesentery           | 114 |
| Ribbert.....             | 1905          | 1    | ?           | Thyroid in "tumor" of ovary                                | .....  | 115 |
| Riebel and Riebel.....   | 1927          | 1    | 33          | Thyroid  | .....  | 116 |
| Ries.....                | 1914          | 1    | ?           | Cystoma with thyroid                                       | .....  | 117 |
| Rothe.....               | 1904          | 2    | 27          | Dermoid with thyroid                                       | Dermoid of opposite ovary                            | 118 |
|                          |               |      |             |  | .....  | 119 |
| Rulz.....                | 1927          | 1    | 45          | Dermoid with thyroid                                       | .....  | 120 |
| Saller.....              | 1943          | 1    | 46          | Thyroid  | Bilateral dermoids previously removed                | 121 |
|                          |               | 2    | 64          | Thyroid  | Ascites  | 122 |
|                          |               |      |             |  | Golter present                                       | 123 |
| Saldi.....               | 1937          | 1    | 36          | Dermoid with thyroid                                       | Golter present                                       | 124 |
| Sanders.....             | 1935          | 1    | 51          | Cystoma with thyroid                                       | .....  | 125 |
| Schauta.....             | 1911          | 1    | 43          | Cystoma (?) with thyroid                                   | .....  | 126 |
| Schlekele.....           | 1911          | 1    | 29          | Cystoma with thyroid                                       | .....  | 127 |
| Schlipper.....           | 1907          | 1    | 51          | Thyroid  | Metastasis to peritoneum and omentum; golter present | 128 |
| Shapiro.....             | 1930          | 1    | 38          | Thyroid  | .....  | 129 |
| Shaw, E. H.....          | 1926          | 1    | 71          | Dermoid with thyroid                                       | .....  | 130 |
| Shaw, W.....             | 1932          | 1    | 34          | Cystoma (?) with thyroid                                   | .....  | 131 |
|                          |               |      |             |  | .....  | 132 |
| Swanton.....             | 1906          | 1    | 42          | Cystoma with thyroid                                       | .....  | 133 |
| Thaler.....              | 1923          | 1    | 40          | Cystoma with thyroid                                       | Dermoid of opposite ovary; ascites                   | 134 |
|                          |               |      |             |  | .....  | 135 |
|                          |               |      |             |  | .....  | 136 |
| Trapl.....               | 1935          | 1    | 29          | Dermoid with thyroid                                       | .....  | 137 |
|                          |               | 2    | 43          | Cystoma with thyroid and endometrioma                      | .....  | 138 |
| Trettenero.....          | 1931          | 1    | 49          | Dermoid with thyroid; pure thyroid tumor of opposite ovary | .....  | 139 |
| Tribedi and De.....      | 1944          | 1    | 25          | Dermoid with thyroid                                       | .....  | 140 |
|                          |               | 2    | 50          | Dermoid with thyroid                                       | .....  | 141 |
|                          |               | 3    | 38          | Bilateral dermoids with thyroid                            | .....  | 142 |
| Ulesko-Stroganowa.....   | 1905          | 1    | 54          | Bilateral pure thyroid tumors                              | .....  | 143 |
| Vagedes.....             | 1904          | 1    | 26          | Cystoma with thyroid                                       | Golter present                                       | 144 |
| Walther.....             | 1903          | 1    | 55          | Dermoid with thyroid                                       | .....  | 145 |
|                          |               | 2    | 33          | Dermoid with thyroid                                       | .....  | 146 |
|                          |               | 3    | ?           | Cystoma with thyroid                                       | Golter present                                       | 147 |

TABLE 2.—*Published Cases of Struma Ovarii—Continued*

| Author                         | Year | Case | Age,<br>Yr. | Pathology                           | Comment  | No. |
|--------------------------------|------|------|-------------|-------------------------------------|--|-----|
| Werth.....                     | 1928 | 1    | 36          | Thyroid with bone and calcification | Implantation of tumor on pelvic peritoneum; ascites                | 143 |
| Wilms.....                     | 1895 | 1S   | 24          | Dermoid with thyroid                | Dermoid of opposite ovary at 18 yr.                                | 144 |
|                                |      | 19   | 52          | Dermoid with thyroid                | .....  | 145 |
|                                | 1896 | 1    | 22          | Teratoma with thyroid               | .....  | 146 |
| Witherspoon.....               | 1932 | 1    | 35          | Dermoid with thyroid                | Dermoid of opposite ovary  | 147 |
| Wood.....                      | 1909 | 1    | ?           | Cystoma with thyroid and bone       | .....  | 148 |
|                                |      | 2    | ?           | Cystoma with thyroid                | .....  | 149 |
|                                |      | 3    | 40          | Cystoma with thyroid                | Histologically "malignant" areas                                   | 150 |
|                                |      | 4    | ?           | Dermoid with thyroid                | .....  | 151 |
| Wynne, McCartney and McClendon | 1940 | 1    | 26          | Thyroid                             | Metastasis to ischium  | 152 |
| Present case.....              | .... | 1    | 58          | Thyroid                             | Adhesions present; tumor thrombi in veins of tumor; goiter present | 153 |

Kretschmar in 1901 reported a cystoma of the ovary containing tissue similar to that described by Gottschalk. Kretschmar was impressed by the intimate relation of the follicles to the lymphatic vessels and at first regarded the tumor as an endothelioma. In a later paper (1904) he identified it as thyroid tissue, which he believed had metastasized to the ovary from the thyroid gland.

In 1902 Pick presented a case of ovarian dermoid containing thyroid and stated that of twenty-one dermoids studied six contained thyroid tissue. He concluded that all ovarian tumors containing thyroid must be teratomatous in origin and assigned them the name "teratoma strumoides thyroideale ovarii." Pick cited the cases of Gottschalk and Kretschmar as examples in which thyroid tissue had developed while all other teratomatous elements were suppressed.

Since this time, only Bauer has seriously questioned the identity of the thyroid tissue. Bauer attempted to show that these tumors are a form of cystadenoma in which a thyroid-like structure is produced by downgrowth of the surface epithelium of the ovary. While this may be the correct interpretation of the particular case described by Bauer, such an explanation does not hold for struma ovarii in general. Nicholson has shown that although many of the published reports of cases are lacking in the detail necessary to a scientific demonstration there is, nevertheless, an abundance of proof that these tumors are composed of genuine thyroid tissue.

It is the purpose of this paper to describe the pathologic changes and functional activity of thyroid tissue in ovarian tumors. This study is based on investigation of a case of struma ovarii and analysis of 152 previously published reports of cases (table 2). While a few reports of cases were inaccessible and no doubt a few were overlooked, it is believed that the total number of published cases cannot be much in excess of 160.

## REPORT OF A CASE

*Clinical Record.*—Mrs. S. C., a 58 year old white housewife was examined Feb. 10, 1940. She had borne ten children, seven alive and three stillborn, and had ceased to menstruate at 49 years of age. Her mother died of cancer of the stomach, and one sister had goiter. Her complaint was of pelvic discomfort, a sense of pressure on the bladder and extreme urinary frequency. Two and one-half years before, her physician had noted the presence of a small nodular goiter associated with loss of weight, nervousness, tachycardia (rate 110) and basal metabolic rate of +19 per cent.

Physical examination showed that her height was 59½ inches (151 cm.), weight 120 pounds (54.4 Kg.), temperature 98.2 F., pulse rate 100; respiratory rate 22 and blood pressure 140 systolic and 80 diastolic. There was no lid lag or exophthalmos. The right lobe of the thyroid was palpable and contained a firm nodule 2 cm. in diameter; the left lobe was barely palpable. On pelvic examination a round hard mass about 5 cm. in diameter could be felt in the left adnexa. A roentgenogram of the chest showed slight ventricular hypertrophy on the left side, a slightly widened aortic arch and some increase in hilar and bronchovascular markings.

Laboratory examination showed a hemoglobin content of 13.3 Gm., erythrocytes 5,000,000 and leukocytes 7,800; the differential count was neutrophils 60 per cent, eosinophils 2 per cent, lymphocytes 32 per cent and monocytes 6 per cent; the sedimentation rate was 26 mm. in one hour (Westergren). Serum reactions to Kahn and Kline tests were negative. Examination of urine gave these findings: acid, quantity not sufficient; albumin, 1 plus, and no sugar. Microscopically there were leukocytes 2 plus and fine granular and hyaline casts 3 plus.

Operation was performed Feb. 27, 1940, with the patient under ether anesthesia. The pelvic organs were exposed through an incision in the lower midline of the abdomen. The greater omentum was found to be densely adherent to the parietal peritoneum; there was no ascites. There was a solid tumor of the left ovary, 5 cm. in diameter, which was well encapsulated and not adherent to any other viscera, except to the fimbriae of the left tube. The right ovary was small and atrophic and appeared normal. There were no signs of peritoneal implantations or metastases. Palpation of organs of the upper part of the abdomen was impossible because of the dense omental adhesions. Bilateral salpingo-oophorectomy and appendectomy were done, and the wound was closed in layers. Convalescence was uneventful, and the patient is alive and well six years later.

*Pathologic Examination.*—The tumor measured 5 by 3 by 4 cm., weighed 45 Gm. and was covered by a dense capsule, which was adherent to the fimbriae of the tube. On section, the tumor was solid, grayish white and of firm consistency. There was a fine trabeculated appearance, with small translucent areas 1 or 2 mm. in diameter between the septums. The remnants of ovarian tissue were visible at one pole and contained several small thin-walled cysts 2 or 3 mm. in diameter.

The tissue was fixed in 5 per cent solution of formaldehyde and embedded in paraffin, and a large number of representative sections were cut. These were stained with hematoxylin and eosin, Kraus's polychrome methylene blue tannic acid colloid stain and mucicarmine.

Microscopically, the tumor consisted of remnants of ovary, differentiated thyroid tissue, thyroid adenoma and small foci of osseous formation. The remnant

of ovary was no more than a thin shell of atrophic ovarian tissue lying on one pole of the thyroid tumor. There were no ovarian follicles; an old corpus albicans was present.

The well differentiated portion of the tumor consisted of follicles filled with homogeneous acid-staining colloid, which exhibited the vacuolization and retraction



Fig. 1.—Junction of ovarian and thyroid tissue. Note the old corpus albicans. Hematoxylin and eosin;  $\times 92$ .

characteristic of thyroid colloid. This colloid stained blue and violet by Kraus's method but was nowhere fuchsinophilic. No mucin or pseudomucin was demonstrable in any part of the tumor by mucicarmine. The follicular epithelium was low columnar in the small follicles, cuboid in the medium-sized follicles and flattened in the large follicles. The diameter of the follicles was determined by actual

measurement of 1,200 vesicles and found to average 70 microns. The stroma was fairly abundant, with numerous fibrous septums producing lobulation. The tissues were well supplied with many small thin-walled blood vessels. Several follicles were observed to be filled with large, foamy phagocytic cells.

The undifferentiated tissue was distributed throughout the tumor, occurring in masses and nodules varying from microscopic size to 8 or 10 mm. in diameter. The



Fig. 2.—Thyroid tissue, area of distinct colloid storage, large follicles and flattened epithelial cells. Hematoxylin and eosin;  $\times 137$ .

cells which made up these masses were closely packed and usually arranged in cords and columns separated from one another by a delicate stroma. In a few places the cells showed a tendency to arrange themselves in a circular fashion and thus form primitive follicles, which in some instances contained a droplet of

colloid. The cells were fairly uniform in size and staining qualities and closely resembled the cuboid cells of the medium-sized follicles. Mitotic figures were rare. These adenomatous areas were actively growing, with rounded borders compressing the adjacent follicles and blending imperceptibly with the interfollicular cells of the more highly differentiated thyroid tissue.



Fig. 3.—Solid area of tumor showing striking epithelial proliferation without colloid storage. Hematoxylin and eosin;  $\times 153$ .

An intermediate grade of differentiation was exhibited in some places where the follicles were irregular in size and shape and contained little colloid. The epithelial cells of these follicles were loose, seemed to fall away frequently from their neighboring cells and by proliferation filled the lumen of many follicles.

Malignant tendencies were indicated by this disorder, by the active proliferation of the adenomatous tissue, by the invasion of the fibrous capsule by epithelial cells

and especially by the invasion of blood vessels by the tumor cells. Numerous instances were noted in which small and medium-sized veins contained thrombi made up in large part of tumor cells, sometimes arranged in follicles containing colloid.

Several foci of osseous formation were present in the tumor, all being of microscopic size. One deposit of calcium was seen. No other tissue was found.

The right ovary showed senile atrophy; the tubes and appendix were normal.

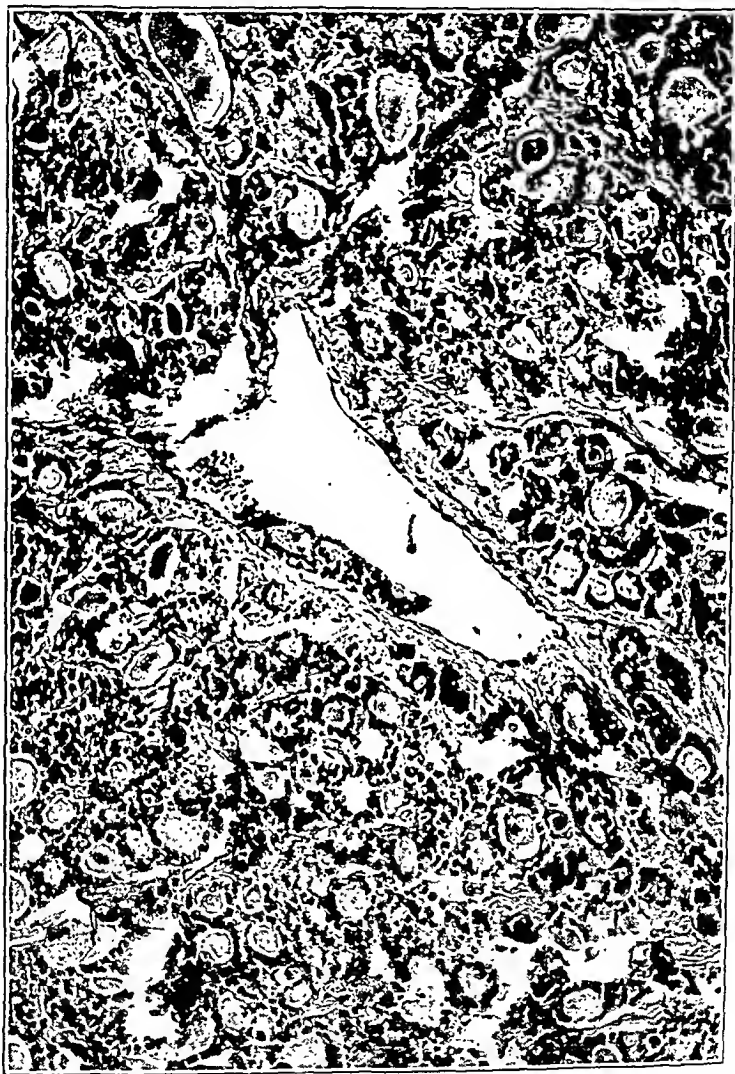


Fig. 4.—Invasion of a large vein by tumor tissue; small follicles predominate in this area, and interfollicular cells are numerous. Hematoxylin and eosin;  $\times 153$ .

*Metabolic Studies.*—The patient's basal metabolic rate was not determined during the immediate preoperative period. A test made two and one-half years previously (June 4, 1937) had shown a rate of  $+19$  per cent. After the histologic character of the tumor had been ascertained, tests were made with results as

follows: June 29, 1940, + 36 per cent and Oct. 24, 1940, + 12 per cent. During this time there was a gain in weight from 118 to 124 pounds (53.5 to 56.2 Kg.).

Determination of the patient's blood iodine content was carried out Oct. 24, 1940, by the method of Davison, Zollinger and Curtis. This test showed the acetone-soluble fraction to be 5.42 micrograms per hundred cubic centimeters of whole blood, water-soluble fraction 0.16 micrograms per hundred cubic centimeters and insoluble fraction 1.18 micrograms per hundred cubic centimeters.

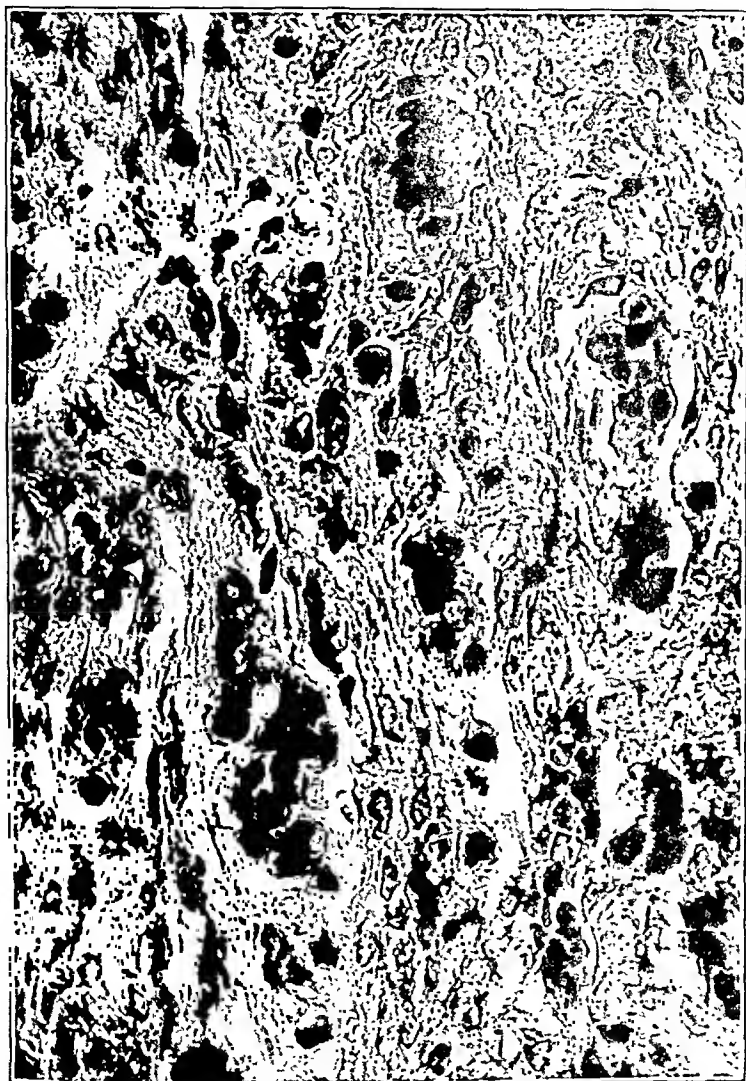


Fig. 5.—Invasion of the narrow fibrous capsule of the tumor by a cluster of epithelial cells. Hematoxylin and eosin;  $\times 369$ .

The estimation of the iodine content of the tumor was performed by the method of Matthews, Curtis and Brode. Eight blocks of tissue were cut from representative portions of the tumor for analysis. The concentration of iodine per hundred grams of tumor tissue (wet weight) varied in these blocks from 1.279 to 5.480 mg. and averaged 2.376 mg.



## PATHOLOGY

1. *Incidence and Types of Tumors.*—Ovarian tumors containing thyroid tissue occur at all ages. Mертtens reported the case of a 6 year old girl and Heinsen that of a woman of 74. The average age in 139 cases was 42 years.



Fig. 6.—Focus of osseous formation in the tumor. Hematoxylin and eosin;  $\times 153$ .

Thyroid tissue occurs in several varieties of ovarian tumor. If the case of Ribbert, who gives no information whatever, is excluded, there are 152 cases, including my own, in which some statement is made concerning the type of tumor present (table 3).

Dermoids constitute the largest group of tumors which exhibit thyroid tissue. Seventy-six of the tabulated cases fall in this group. In some of the cases the author has given a clear objective description which leaves no doubt that he was dealing with a dermoid or teratoma composed of multiple tissues. In other cases there is only the author's statement that the tumor was a dermoid or teratoma. Many of the dermoids were associated with a cystoma of the serous or pseudomucinous variety.

In 47 cases a serous or pseudomucinous cyst has been described in combination with a solid tumor consisting of thyroid tissue without other recognizable teratomatous elements. Tumors have been included in this group even though bone or cartilage has been found, for the reason that these tissues may arise anywhere in the body and are not necessarily characteristic of teratomas.

Thyroid tumors occurring alone, without cystoma and without other teratomatous elements (but not excepting bone or cartilage),

TABLE 3.—*Varieties of Struma Ovarii*

| Pathologic Conditions     | Cases | Per Cent |
|---------------------------|-------|----------|
| Dermoid with thyroid..... | 76    | 50       |
| Cystoma with thyroid..... | 47    | 31       |
| "Pure" thyroid.....       | 26    | 17       |
| Miscellaneous.....        | 3     | 2        |

are listed twenty-six times in the series. These are the cases of so-called pure struma ovarii; the present specimen falls into this classification. The smallest tumor of this sort was a 6 mm. nodule of thyroid tissue found by Masson and Mueller at autopsy of a 38 year old woman who died of thyrotoxicosis and hepatic atrophy. Some of these tumors have reached considerable size, tumors the "size of a child's head" having been reported by Gottschalk (1899) and Ulesko-Stroganowa.

There remain 3 special cases which cannot be classified with any of the preceding groups. Frankl (1931 and 1934) described a thyroid tumor with a Brenner tumor of the same ovary and a granulosa cell tumor of the opposite ovary. Gargano described a tumor weighing 1.5 kg. removed from a 45 year old woman; the tumor consisted mostly of thyroid, but in some areas epithelial syncytia were present which were typical of chorionic carcinoma. The patient exhibited many tumor implants over the omentum and died five months after the operation. Finally, in Trapl's second case the growth consisted of a cystoma with thyroid tissue and an endometrial inclusion.

2. *Tumors of the Opposite Ovary.*—A tumor of the opposite ovary has been reported in 21 cases of struma ovarii. Thyroid tissue was

present bilaterally in 6 cases, or approximately 4 per cent of the series. The pathologic types of bilateral tumors which have been described are recorded in table 4.

3. *Ascites and Adhesions*.—Ascitic fluid was found in 26 cases, or 17 per cent, and adhesions are mentioned five times in the literature. My own patient did not have ascites, but adhesions were conspicuous. These findings cannot be considered indicative of malignant growth, as they are frequently found with other benign ovarian tumors. Thus, Cabot found ascites in 7.9 per cent of ovarian cystomas; though this frequent association of benign ovarian tumors with ascites is well known, its cause is not yet understood.

TABLE 4.—*Thyroid Tissue in Association with Bilateral Ovarian Tumors*

| Author                         | Type of Principal Tumor     | Tumor of Opposite Ovary |
|--------------------------------|-----------------------------|-------------------------|
| 1. Plaut.....                  | Cystoma with thyroid        | Cystoma                 |
| 2. Fiebach.....                | Cystoma with thyroid        | Cystoma                 |
| 3. Thaler.....                 | Cystoma with thyroid        | Dermoid                 |
| 4. Ulesko-Stroganowa.....      | Thyroid                     | Thyroid                 |
| 5. Boxer.....                  | Thyroid                     | Dermoid                 |
| 6. Saller.....                 | Thyroid                     | Dermoid                 |
| 7. Moench.....                 | Dermoid with thyroid        | Cystoma                 |
| 8. Alsenstadt.....             | Dermoid with thyroid        | Cystoma                 |
| 9. Frankl (1924).....          | Dermoid with thyroid        | Cystoma                 |
| 10. Murray and associates..... | Dermoid with thyroid        | Granulosa cell tumor    |
| 11. Manasse.....               | Dermoid with thyroid        | Dermoid with thyroid    |
| 12. Morgen.....                | Dermoid with thyroid        | Dermoid with thyroid    |
| 13. Giannettasio.....          | Dermoid with thyroid        | Dermoid with thyroid    |
| 14. Tribedi and De.....        | Dermoid with thyroid        | Dermoid with thyroid    |
| 15. Rothe.....                 | Dermoid with thyroid        | Dermoid                 |
| 16. Adolf.....                 | Dermoid with thyroid        | Dermoid                 |
| 17. Witherspoon.....           | Dermoid with thyroid        | Dermoid                 |
| 18. Macleod.....               | Dermoid with thyroid        | Dermoid                 |
| 19. Wilms (1895).....          | Dermoid with thyroid        | Dermoid                 |
| 20. Trettenero.....            | Dermoid with thyroid        | Thyroid                 |
| 21. Frankl (1931).....         | Thyroid with Brenner tumor, | Granulosa cell tumor    |

4. *Metastasis*.—Dissemination of these tumors has occurred in a few instances.<sup>2</sup> Three distinct types of metastasis have been found: local implants on the peritoneum and omentum (Morgen, Shapiro, Werth and Emge), regional spread, with nodules in the liver (Proescher and Roddy [third case] and Mohr), and distant metastasis to bone via the blood stream (Eerland and Wynne, McCartney and McClendon). The local implants may be benign and not incompatible with a long survival period (Morgen's patient lived eighteen and one-half years). Proescher and Roddy's patient with metastasis to the liver showed recurrence in five months and died in one year; Mohr's patient died on the fifteenth postoperative day. Skeletal metastasis may be highly

2. It is to be noted that Ulesko-Stroganowa's case of "metastasis" of pure struma from one ovary to the other is not included. It is apparent from my tabulation that bilateral teratomas are not rare, and without other evidence of metastasis such an explanation is extremely unlikely.

malignant, as in Eerland's case, or relatively benign, as in the case of Wynne and associates, in which a metastasis to the ischium was removed surgically and no recurrence had been noted within six months.

Gargano has reported the surgical removal of a 1,500 Gm. tumor from a 45 year old woman; there were numerous nodules in the omentum, and the patient died five months after operation; autopsy was not performed. Microscopic examination of the tumor showed it to be composed principally of thyroid, which was combined with a chorionic carcinoma. It is not clear whether the malignity is to be attributed entirely to the chorionic carcinoma or whether there was also dissemination of the thyroid tissue.

5. *Coincidence of Cervical Goiter and Struma Ovarii.*—Cervical goiter has been recorded twenty-five times in the entire series of 153 cases, an incidence of 16.3 per cent. Since many of the reports of cases in the literature do not provide a complete clinical description of the patient, the true incidence of goiter with struma ovarii is probably higher.

6. *The Cellular Pathology of the Thyroid Tissue in Struma Ovarii.*—The usual histologic changes of struma ovarii appear to have been well illustrated in my own case. Point by point, the tissue is identical with the structure of the thyroid gland. There are the same rounded follicles, lined with cubical or flattened epithelium. The colloid is homogeneous, tends to retract from the epithelium and is frequently vacuolated. The staining qualities are those of colloid, not mucin or pseudomucin. The stroma is delicate, and interfollicular cells are numerous. There is evidence of various levels of physiologic activity, with a few large cystic follicles filled with colloid and in other places a somewhat hyperplastic gland with many small follicles.

The parallel extends farther. The tumor exhibits not only the differentiated architecture of adult thyroid tissue but also the proliferation and disorganization of a malignant thyroid adenoma. The potentially malignant nature is clearly shown by the numerous vessels containing tumor cells. That metastasis did not occur prior to operation seems remarkable, and one can only presume that such cells as may have been transported by the blood stream did not find a suitable site or did not possess sufficient vitality to establish a metastatic focus.

A histologic appearance of malignant growth has been described repeatedly. Gottschalk (1899) described his specimen as similar to "struma maligna." Such reports must be examined in the light of modern knowledge of thyroid neoplasia. Histologic criteria of malignant growths of the thyroid are not so easily formulated as for most epithelial organs. This difficulty arises from the structure of the gland itself, which consists of epithelial follicles set directly on the

stroma, without any basement membrane. Between the follicles lie the undifferentiated interfollicular cells, capable of proliferation and organization in response to a suitable physiologic stimulus. The borderline between physiologic and neoplastic processes is still vague. Adenomas occurring in the thyroid show various grades of differentiation and organization. Graham considered invasion of the blood vessels the only reliable distinction between benign and malignant adenomas.

Adenomatous proliferation with struma ovarii has been described and illustrated by Frankl (1914). In his case there was a solid cellular growth separated from the rest of the thyroid tissue by a fibrous septum. Norris described proliferation and anaplasia suggesting malignant growth. Moench (1929) illustrated in his first case what he considered to be typical adenocarcinoma; Plaut's first case (1933) contained a carcinoma-like solid tumor. In none of these cases was invasion of the blood vessels or metastasis demonstrated.

However, invasion of the blood vessels has long been recognized. Kroemer ("Handbuch der Gynäkologie") cited Ribbert's opinion that this, rather than a particular alteration of parenchymatous cells, is the important criterion in the recognition of malignant growth. Kretschmar (1901) described an intimate blending of capillaries and gland epithelium. Wynne, McCartney and McClendon observed an area of adenocarcinoma with possible invasion of the blood vessels. Apparently, mine is the first report to illustrate clearly this important criterion of malignant growth by photomicrographs.

Papillary tumors arising in struma ovarii have been reported by Manasse and Morgen. Morgen regarded his case as homologous to the papillary tumors which arise from the cervical thyroid and from so-called lateral aberrant thyroids.

*7. Calcification and Ossification.*—In tabulation of the different types of ovarian tumors associated with thyroid tissue, note was taken of the fact that some of the otherwise pure thyroid or cystoma with thyroid tumors contained foci of calcification or formation of bone or cartilage. Since bone and cartilage may develop widely in the body, we agree with Nicholson in excluding this as a special quality of teratomas. Kaufmann stated that calcification and ossification are fairly frequent in cervical goiters. Bone is mentioned in 3 of 26 cases of "pure" struma ovarii (Meyer, Werth and this case), an incidence of 11.5 per cent; it was recorded in 5 of 47 cases of thyroid tissue associated with cystoma (Kretschmar, Proescher and Roddy [second case], Wood [first case], Neumann [second case] and Heinsen), an incidence of 10.6 per cent. Neumann and Heinsen also mentioned the presence of cartilage. My own experience is significant in that the foci of osseous formation were microscopic in size and found only after a careful search of many

sections. No doubt, serial sections in every case would reveal a much higher incidence of formation of bone and cartilage than has been recorded in the literature.

## PHYSIOLOGY

1. *The Iodine Content of Struma Ovarii.*—Investigation of the iodine content of the thyroid tissue has been undertaken in 32 cases. Fifteen were reported as negative (Adolf [2 cases], Bauer, Bua,

TABLE 5.—*Iodine Content in Struma Ovarii*

| Investigator                      | Case | Pathology               | Published Data            |                                       | Mg. of Iodine/<br>Gm. of Tissue |        |
|-----------------------------------|------|-------------------------|---------------------------|---------------------------------------|---------------------------------|--------|
|                                   |      |                         | Method of<br>Iodine Assay | Quantity                              | Wet                             | Dry    |
| Brandenburg.....                  | 1    | Dermoid with<br>thyroid | .....                     | 0.214 mg./Gm.<br>dry tissue           | .....                           | 0.214  |
| Emge.....                         | 2    | Cystoma with<br>thyroid | Hilty and<br>Wilson       | 1.055 mg./Gm. (average)<br>wet tissue |                                 |        |
|                                   |      |                         |                           | 0.982 mg./Gm.<br>wet tissue           | 1.018                           |        |
|                                   |      |                         | Matthews and<br>Curtis *  | 0.085 mg./Gm.<br>wet tissue           | 0.085                           |        |
| King and Norris.....              | 1    | Cystoma with<br>thyroid | Pickworth                 | 11.1 mg./100<br>Gm. dry tissue        | .....                           | 0.111  |
|                                   | 2    | Dermoid with<br>thyroid | Pickworth                 | 12.8 mg./100<br>Gm. dry tissue        | .....                           | 0.128  |
| Macleod.....                      | 1    | Dermoid with<br>thyroid | von Fellenburg            | 7.8 mg./100 Gm.<br>wet tissue         | 0.078                           |        |
| Masson and Mueller                | 1    | Cystoma with<br>thyroid | .....                     | 0.105% dry<br>weight                  | .....                           | 1.05   |
|                                   | 3    | Pure thyroid            | .....                     | 0.031% dry<br>weight                  | .....                           | 0.31   |
|                                   | 4    | Thyroid and<br>cystoma  | .....                     | 0.011% dry<br>weight                  | .....                           | 0.11   |
| Meyer.....                        | 1    | Pure thyroid            | Baumann-<br>Oswald        | 1.37 mg./100<br>Gm. ash (?)           | .....                           | 0.0137 |
| Xeu.....                          | 1    | Cystoma with<br>thyroid | .....                     | 0.02 mg./Gm.<br>wet tissue            | 0.02                            |        |
| Plaut.....                        | 1    | Cystoma with<br>thyroid | Kendall and<br>Richardson | 0.673 mg./100<br>Gm. wet tissue       | 0.0067                          |        |
|                                   | 2    | Cystoma with<br>thyroid | Kendall and<br>Richardson | 0.025 mg./100<br>Gm. wet tissue       | 0.00025                         |        |
| Shapiro.....                      | 1    | Pure thyroid            | .....                     | 8.69 mg./100 Gm.<br>dry tissue        | .....                           | 0.0869 |
| Wynne, McCartney<br>and McClendon | 1    | Pure thyroid            | McClendon and<br>Bratton  | 2.25 mg./100<br>Gm. wet tissue        | 0.0225                          |        |
| Present case.....                 | 1    | Pure thyroid            | Matthews and<br>Curtis    | 2.4 mg./100<br>Gm. wet tissue         | 0.024                           |        |

\* The discrepancy in results obtained in analysis by the two methods may be attributed to the fact that different laboratories using different methods do not obtain strictly comparable values in iodine analysis. Hilty and Wilson's method is a dry ash procedure, while that of Matthews and Curtis is a wet ash method; the dry ash method is known to give higher results than most wet ash procedures.

Heinsen, Kafka [3 cases], Kretschmar, Moench [3 cases], Nicholson, Plaut [third case] and Ulesko-Stroganowa); qualitative tests were reported as giving positive results in 2 cases (Schauta and Wood). Fifteen quantitative determinations have demonstrated iodine in varying amounts (table 5). Results are not strictly comparable, as different methods have been employed and some are recorded in terms of wet

tissue and others on the basis of dry weight. The maximum values recorded are those of Emge, 1.018 mg. of iodine per gram of wet tissue, and of Masson and Mueller's first case, 1.05 mg. of iodine per gram of dry weight. These concentrations correspond to the iodine content of the normal adult thyroid gland. Most of the reports, however, show small quantities of iodine, indicating that iodine storage is minimal in the majority of these tumors. All the reports listed in table 5 show significant amounts of iodine except Plaut's second case, which is in the same range as the usual concentration of iodine in the ovary (30 to 160 micrograms per hundred grams).

## 2. *Biologic Evidence of Physiologic Activity of Struma Ovarii.*—

Plaut studied the physiologic activity of these tumors by means of biologic tests. He investigated three tumors and found that the acetonitril reaction and the reaction to the tadpole test were positive in two tumors containing iodine; the reactions were negative in the third case, in which no iodine was found. Kleine found the Reid Hunt reaction positive in his sixth case but denied that the test was of an intensity characteristic of thyroid. Plaut's results indicate that in struma ovarii, as in the thyroid gland, the biologic activity parallels the iodine content.

## 3. *Clinical Evidence of Physiologic Activity of Struma Ovarii.*—

Symptoms of thyrotoxicosis have been frequently cited as evidence of the physiologic activity of struma ovarii. In many cases the data are wholly inadequate and cannot be regarded as significant. In other cases there was an associated goiter present, which may have been partially or wholly responsible for the symptoms noted. Including my own, 17 patients have shown symptoms of thyrotoxicosis. Of these I should delete those of Moench (1929), Saidl and Aschkanasy for insufficient data. The symptoms in 2 cases (Kovacs, Cantor and Kogut) subsided before any operation was done. In 4 cases, including my own (Brandenburg and Masson and Mueller [cases 1 and 5]), there was a cervical goiter present, which could have accounted for the symptoms. Seven patients (Castano, Emge [cases 1 and 2], Hundley, Kleine [case 6], Neumann [case 3] and Gusberg and Danforth) seem to have shown significant alleviation of symptoms following operation. Masson and Mueller's second case cannot be interpreted as there was an elevated basal metabolic rate after operation but no goiter is mentioned. Neumann's case presents the interesting but puzzling observation that the struma colli diminished in size and the thyrotoxic symptoms abated after removal of the tumor. The published data are summarized in table 6.

It is worthy of comment that thyroid intoxication is dependent on more than an increase in the mass of thyroid tissue contained in the body. The functional activity of the thyroid gland is largely regu-

TABLE 6.—Symptoms of Thyrotoxicosis Associated with Struma Ovarii

| Investigator              | Case | Symptoms   | Basal Metabolic Rate   | Comment  |
|---------------------------|------|--|--|--|
| Atchkanasy.....           | 3    | Sweats, palpitation and diarrhea   | .....  | Symptoms not improved by removal of tumor, though basal metabolic rate fell temporarily to +6.6; thyroidectomy done, with relief   |
| Brandenburg.....          | 1    | Loss of weight, palpitation, dyspnea and tachycardia   | +29.8  | Patient 2 mo. pregnant at operation; normal delivery at term   |
| Canfor and Kogut.....     | 1    | Tachycardia, sweats; exophthalmos present 3 yr. previously   | .....  | Basal metabolic rate fell to +10 after operation   |
| Castano.....              | 1    | Pulse rate 110   | +36  | Basal metabolic rate fell to -14 after operation; symptoms relieved  |
| Emge.....                 | 1    | Tachycardia  | +12 to +34   | Removal of omental metastases resulted in relief of symptoms; basal metabolic rate +4  |
| Hundley.....              | 2    | Tachycardia; loss of weight; exophthalmos  | +6.3 to +16.5 postoperative  | Basal metabolic rate not reduced by subtotal thyroidectomy but fell to -6 after removal of tumor   |
|                           | 1    | Fine tremor  | +22 and +42 before operation; +30 after subtotal thyroidectomy                               |  |
| Kleine.....               | 6    | Thyrototoxic   | .....  | Serum Reid-Hunt reaction positive before operation and negative after removal of tumor   |
| Kovacs.....               | 1    | Exophthalmos; patient previously showed signs of thyrotoxicosis, but these subsided before operation | .....  |  |
| Masson and Mueller.....   | 1    | Thyrototoxic   | +15  | Basal metabolic rate -4 after subtotal thyroidectomy and removal of tumor  |
|                           | 2    | Thyrototoxic   | No preoperative determination  | Basal metabolic rate +32 and +30 postoperatively   |
|                           | 5    | Severe thyrotoxicosis; patient died from thyrotoxicosis and atrophy of liver                         | +47 to +82   | Parenchymatous goiter present; ovarian thyroid 6 mm. in diameter found at autopsy  |
| Moench.....               | 3    | Fine tremor, irregular action of heart   | .....  | Symptoms relieved by operation; no iodine found in tumor   |
| Neumann.....              | 3    | Thyrototoxic   | +40  | Blood iodine 35 micrograms per 100 cc. before operation; struma colli diminished in size; basal metabolic rate returned to normal and symptoms relieved after removal of tumor |
| Siddl.....                | 1    | Tachycardia, tremor  | .....  | Large cervical goiter; blood iodine 15.1 micrograms per 100 cc. before operation; thyroidectomy performed; colloid goiter found  |
| Gusberg and Dunforth..... | 1    | Palpitation, perspiration, nervousness, slight tremor and tachycardia                                | +30 to +60 before thyroidectomy; +10 after thyroidectomy; -14 after removal of struma ovarii |  |
| Author's case.....        | 1    | Tachycardia, loss of weight and nervousness  | +19 (determination made 2½ yr. prior to operation)   | No apparent relief from removal of tumor; symptoms attributed to coexisting toxic nodular goiter; symptoms have gradually subsided   |



lated by extrathyroid factors. Presumably, the ovarian thyroid falls under the influence of these same regulatory factors; to what degree a tumor of this sort may function autonomously is not known.

#### THE ORIGIN AND NATURE OF STRUMA OVARII

The origin of thyroid tissue in ovarian tumors has been explained in various ways. It has been denied that the tissue is true thyroid. Gottschalk considered the tumor a "folliculoma" arising from ovarian follicles. Bauer was able to discern what he regarded as evidence of the origin of the tumor by invagination of the covering epithelium (mesothelium) of the ovary. Finding no iodine in the tumor, he concluded that it was a cystadenoma bearing a structural resemblance to thyroid and asserted his belief that every so-called struma ovarii was in reality a cystadenoma. In the light of the histologic studies and evidence of physiologic activity which I have cited, such a view is no longer tenable. Architecturally and physiologically, these tumors are composed of genuine thyroid tissue.

In approximately half of the cases of struma ovarii, the tumors exhibit other tissues obviously foreign to the ovary. These tumors belong to the general class of teratomas; those containing hair, sebaceous glands, sweat glands or teeth may properly be referred to as dermoids. In such tumors the thyroid is but one of several well differentiated tissues; the presence of thyroid is no more remarkable than the occurrence of digestive epithelium or brain tissue.

The ovarian tumors which contain only thyroid or thyroid with a cystoma are generally considered to be teratomas in which all other tissues have undergone regression. This explanation was first advanced by Pick. That a teratoma may undergo extensive reduction in its constituent tissues is shown by Saxer's case, in which a tooth was found in an otherwise normal ovary.

Plausible as this theory is, there is no objective evidence of this regression of tissues in struma ovarii. Teratomas differ from other tumors in the greater potencies of their cells of origin (I do not propose to argue here which cells give rise to teratomas). Growth having been initiated in those cells, differentiation and organization can proceed along various lines. It is no longer necessary to suppose that definitive entodermal cells must precede the development of thyroid tissue; experimental embryology has demonstrated that the primary germ layers are not specific for the tissues which they usually produce. A teratoma is in no sense a fetus and so need not contain multiple tissues developing from specific germ layers. Rather, it may consist, as in the case of pure struma ovarii, of cells organizing and developing into one tissue only. Whether this is due to a primarily unidirectional stimulus or to

suppression of all other cell potencies or to actual overgrowth, with extinction of cells initiating other tissues, is not known.

#### SUMMARY

1. The historical background of struma ovarii is briefly reviewed.
2. A case of "pure" thyroid tumor of the ovary is reported. The tumor was found to consist of thyroid tissue in various grades of differentiation, with malignant invasion of the blood vessels; several foci of osseous formation were observed. The iodine content of the tumor was 2.4 mg. per hundred grams of wet weight. There was evidence of a mild thyrotoxicosis which is attributed to the coexistence of a nodular goiter.
3. The literature has been reviewed and 152 reported cases tabulated.
4. The average age incidence of struma ovarii is 42 years.
5. Cervical goiter has been found associated with struma ovarii in 16.3 per cent of the cases.
6. Ascites and peritoneal adhesions are frequently associated with these tumors.
7. Tumors of the ovary containing thyroid are of three general varieties: dermoids with thyroid, 50 per cent; cystoma with thyroid, 31 per cent, and pure thyroid, 17 per cent. Thyroid tissue has also been observed in association with chorionic carcinoma of the ovary and with a Brenner tumor. Coexisting tumors of the opposite ovary are not infrequent; thyroid tissue has been found bilaterally in 6 instances.
8. Although the majority of these tumors are benign, dissemination has been observed in 8 instances (5.3 per cent). Metastasis may be local, by implantation, or distant, as to the liver or skeletal system.
9. Histologically, struma ovarii reproduces the architecture of the thyroid gland in its normal physiologic variations. Rarely it may exhibit evidence of malignant growth in the form of malignant adenoma, papillary tumor or general anaplasia.
10. Physiologic activity of these tumors is demonstrated by the presence of iodine in approximately half of the tumors investigated, by the presence of thyroid hormone, as determined by the tadpole test, and, in a few instances, by clinical symptoms of thyrotoxicosis, relieved by the removal of the tumor.
11. All tumors of the ovary containing thyroid tissue are now considered to be teratomatous in nature.

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## SURGICAL TREATMENT OF NEOPLASTIC OBSTRUCTION OF THE EXTRAHEPATIC BILIARY TRACT

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LOS ANGELES

TUMORS obstructing the common and hepatic bile ducts include primary neoplasms of the ducts and of the ampulla and carcinoma of the pancreas secondarily involving the common duct. Benign adenomas, polyps and congenital cysts may involve the ducts; however, carcinoma is relatively more frequent, and of this group carcinoma of the ampulla of Vater is perhaps the commonest.<sup>1</sup> All these primary lesions are extremely rare. Kelznack found two instances in four thousand, five hundred and seventy-eight routine postmortem examinations, and McGlinn found five in nine thousand. Of twenty-two thousand operations on the biliary tract at the Mayo Clinic, only forty-one were for carcinoma of the bile ducts.<sup>2</sup> The lesion occurs more frequently among men, and in about half of the cases it is associated with stones in the gallbladder or in the bile ducts. Primary carcinoma most frequently occurs at the junction of the cystic and common ducts or at the division of the common duct into its right and left branches. Occasionally the lesion is localized distal to the cystic duct, in which case it may be excised. Even when the lesion is in this favorable location, resection seldom results in permanent cure, although the procedure is justified on the basis of relieving jaundice and prolonging life. Of the group of 41 patients operated on for carcinoma of the bile ducts, only 1 is still alive and well. In this patient the lesion was localized, and it was excised by W. J. Mayo in 1927.

Early carcinoma or benign papilloma of the ampulla of Vater is usually amenable to local transduodenal excision. Small papillary carcinomas of the ampulla are usually of a low degree of malignancy, producing symptoms early and metastasizing late. For this reason radical procedures, such as the Whipple operation, are not justified in these cases. Aside from these lesions of the ampulla, the picture

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Read at the sectional meeting of the American College of Surgeons, April 18, 1946, at Los Angeles.

1. Cole, W. H., and Elman, R.: *Textbook of General Surgery*, New York, D. Appleton-Century Company, Inc., 1939, p. 598.

2. Walters, W., in Christopher, F.: *Textbook of Surgery*, Philadelphia, W. B. Saunders Company, 1936, pp. 1334 and 1338.

as a whole, from the standpoint of permanent cure, is discouraging. Clagett, Counseller and Waugh, in their report of biliary surgery for 1942, 1943 and 1944 at the Mayo Clinic, made the statement that primary malignant lesions of the biliary tract are not amenable to surgical treatment.<sup>3</sup> Since most carcinomas of the bile ducts are located at or proximal to the cystic duct and since prognosis is fatal in these cases, procedures used for benign stricture, such as vitallium tubes and transplantation of external biliary fistulas, are not practical.

Secondary involvement or compression of the distal common duct offers a more hopeful outlook since the advent of the Whipple type of procedure. The duodenum and the head of the pancreas are resected, and the relief of biliary obstruction is made by anastomosing the gall-bladder or the common duct to a portion of the proximal part of the gastrointestinal tract. Possibilities in this field of surgery are still being explored, and they continue to offer promise. Dixon recently reported a case in which he removed the entire pancreas for an extensive carcinoma of this organ.<sup>4</sup> The patient was living fifteen months after operation. The resultant diabetes was controlled by insulin.

When these factors are considered, the scope of surgical procedure for neoplastic obstruction of the extrahepatic biliary tract is limited essentially to four procedures: 1. Resection of the common duct is done when the lesion is localized to a portion of the duct distal to the cystic duct. If end to end anastomosis is not possible, the proximal portion of the duct may be transplanted into the duodenum, jejunum or stomach. 2. Transduodenal resection of the ampulla of Vater is performed for small benign or malignant papillomas of the ampulla. 3. A Whipple type of procedure is used for carcinoma of the pancreas and the more extensive carcinomas of the ampulla and distal common duct. 4. A palliative bile-shunting operation is done for inoperable malignant growths involving the distal common duct primarily or secondarily.

Four cases are reported which illustrate the procedures used and recommended in each of these types of cases.

#### REPORT OF CASES

CASE 1.—A white woman aged 65 years was aware of jaundice only two and one-half weeks before her admission to the hospital, although she stated that she had considerable itching of the skin for an indefinite time. She also complained of tenderness under the rib margin on the right side. She stated that her stools had been clay colored for some time. She had lost 10 pounds (4.5 Kg.) in weight

3. Clagett, O. T.; Counseller, V. S., and Waugh, J. M.: Proc. Staff Meet., Mayo Clin. **21**:5-10, 1946.

4. Waugh, J. M.; Dixon, C. F.; Clagett, O. T.; Bollman, J. L.; Sprague, R. G., and Comfort, M. W.: Proc. Staff Meet., Mayo Clin. **21**:25-46, 1946.

during the past month. She complained of indigestion but at no time had suffered from colic.

Physical examination revealed a fairly well nourished elderly woman who was extremely jaundiced. A tender mass was palpated in the region of the gallbladder. The icterus index was .182 units, the van den Bergh reaction was directly positive, the prothrombin time was twenty-six seconds and the albumin-globulin ratio was reversed (albumin 3.3 Gm. and globulin 5.65 Gm. per hundred cubic centimeters). The urine contained bile but was otherwise normal. Other physical findings were irrelevant. The preoperative diagnosis was probable carcinoma of the head of the pancreas.

Operation was done on Jan. 28, 1944. A paris green type of liver was found, and the gallbladder was greatly enlarged and full of stones. A friable lesion of the common duct distal to the cystic duct was resected. Continuity of the common duct was reestablished by end to end anastomosis over the proximal portion of the T tube. The tube was inserted into the duct through an opening distal to the site of the anastomosis. A cholecystostomy was made, a dressed tube being used. The diagnosis according to the pathologic report on the section of the common duct removed was grade II adenocarcinoma of the bile duct (type B Duke).

When the patient was dismissed from the hospital, one month later, the stools were bile colored. Cholangiography showed diodrast passing into the duodenum. The hepatic ducts were not dilated, and the gallbladder was visualized. The icterus index was 31 units. Ten months later, symptoms recurred and the patient died. Postmortem examination revealed carcinoma completely obstructing both hepatic ducts.

CASE 2.—A white woman aged 63 years complained of indigestion and painless jaundice for approximately one month. The jaundice steadily increased and was accompanied with pronounced pruritus. She stated that her stools were clay colored and that she had lost weight.

Physical examination showed a thin elderly woman who was deeply jaundiced. The liver was palpated 4 cm. below the costal margin, and an enlarged gallbladder was palpated. The prothrombin time was twenty-two seconds, the icterus index was 126 units and the van den Bergh reaction was directly positive. The albumin-globulin ratio was 1.1, with a normal total protein content. The preoperative diagnosis was obstruction of the common duct.

Operation was done on Feb. 29, 1944. The liver was enlarged, and grossly diffuse hepatitis was evident. No stones were palpated in the gallbladder, and exploration of the common duct did not reveal a stone. White bile drained from the common duct. The duodenum was opened, and a small papilloma of the ampulla of Vater was removed. A cautery resection of the ampulla, including the papilloma, was made, and the common duct was sutured to the duodenum. The opening in the duodenum was closed transversely, and a T tube was sutured in the common duct. According to the pathologic report the tumor was a benign papilloma of the ampulla of Vater.

On the fifth postoperative day the stools became light brown in color. The patient was dismissed from the hospital on the tenth postoperative day. The icterus index was 99.6 units. The report of the cholangiogram on dismissal revealed normal functioning of the extrahepatic biliary system. The referring physician reported that the patient died one year and eight months later. The postmortem diagnosis was cirrhosis of the liver, inflammatory obstruction of the



hepatic duct and carcinoma of the kidney. The jaundice subsided but never completely cleared up.

CASE 3.—A white man aged 39 years complained of painless jaundice, pruritus and epigastric distress for three months. He had lost 40 pounds (18.1 Kg.) in weight during this period. He stated that he had had some fever.

Physical examination revealed an emaciated, deeply jaundiced man. A tender mass was palpated in the upper part of the right side of the abdomen, which was believed to be the gallbladder. The sedimentation rate was 29 mm. in one hour, the urine contained bile and the icterus index was 145 units. Roentgenograms showed an indentation of the second and third portions of the duodenum. A diagnosis of carcinoma of the head of the pancreas was made.

Operation was performed on Sept. 20, 1945. An extensive carcinoma involving the distal part of the common duct and the head and body of the pancreas was found. Since there was no evidence of distant metastasis, a one stage modified Whipple operation was carried out. All but a small portion of the tail of the pancreas was removed. The patient was given 1,500 cc. of blood continuously during the operation, which lasted three and one-half hours.

The convalescence was essentially uneventful. On the fifth postoperative day the icterus index was 120 units, the serum amylase content 800 units and the blood sugar content 73 mg. On the fourteenth postoperative day the patient was entirely ambulatory, the stools contained bile despite an icterus index of 117 units and the serum amylase level had decreased to 400 units. In a follow-up letter from the patient's doctor three months following the operation, it was reported that the icterus index was 15.9 units and serum amylase content 267 units and that all routine laboratory data were normal. A second follow-up letter just received, six months postoperatively, reports that the patient is in good general health and has regained his lost weight and that 18 pounds (8.2 Kg.) of this loss of weight had been gained during the past two months. He has had occasional mild episodes of indigestion, which have subsided with the oral administration of pancreatin. His stools are reported to be normal in color, and he has had no jaundice. His serum amylase content is now 200 units, the blood sugar content 100 mg. and the icterus index 6 units.

CASE 4.—A white woman aged 48 years complained that during the four months prior to her admission to the hospital she had suffered from painless jaundice, pruritus, clay-colored stools and loss of weight.

Physical examination revealed a middle-aged, undernourished woman intensely jaundiced. A tender mass was palpated in the upper right quadrant which was consistent with an enlarged gallbladder. The icterus index was 90 units, and there was an immediate direct van den Bergh reaction in five seconds. A diagnosis of probable carcinoma of the head of the pancreas was made.

Operation was performed Sept. 14, 1939. An inoperable carcinoma which was primary in the head of the pancreas was found. A Rous type of cholecystojejunostomy was made. Convalescence was uneventful until the seventh postoperative day, when fulminating type III pneumonia developed, and the patient died within forty-eight hours.

#### COMMENT

Although the outlook for cure is not bright following surgical procedures for primary malignant growths of the common duct, such procedures may lengthen the life and enhance the comfort of the patient.

An occasional cure may be expected. In the case in which a localized carcinoma of the common duct was resected, the patient lived in comfort for ten months. From a technical standpoint it seems that the simplest and safest method of restoring continuity of the common duct is anastomosis over a T tube. This offers the advantage of subsequent removal of the tube and assurance that a foreign body is not left in the common duct. The tube should be inserted in the duct through an opening distal to the site of the anastomosis, to preclude the danger of separating the anastomosis when the tube is pulled out.

In the case in which the ampulla and a portion of the common duct were removed, the section was so small that the common duct could easily be sutured to the wall of the duodenum without transplantation.

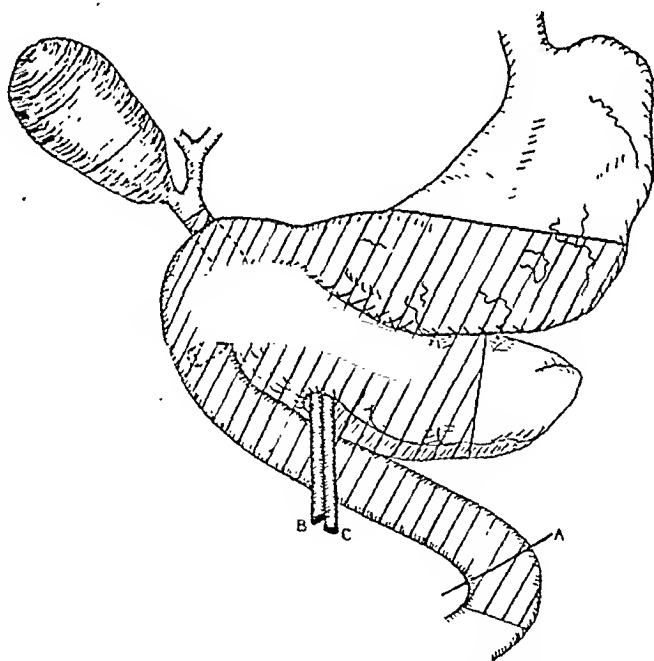


Fig. 1 (case 3).—The deeply shaded area indicates the extent of carcinoma of the pancreas. The lightly shaded area indicates the portion of the stomach, the duodenum, the common duct and the pancreas removed. *A*, ligament of Treitz; *B*, superior mesenteric vein; *C*, superior mesenteric artery.

In view of the fact that the jaundice never completely subsided for eighteen months, it appears that hepatitis with cirrhosis of the liver was an important factor in this case. The degree in which the papilloma of the ampulla contributed to the symptomatology directly or indirectly is problematic. The pathologic condition in the liver being excluded, a case of this type should offer an excellent prognosis for permanent cure.

In a case such as the one in which palliative cholecystojejunostomy was performed, a Rous type of anastomosis is preferable to the loop

type, as the incidence of contamination of the gallbladder with intestinal contents is lessened. Even with the Rous procedure it is advisable to make valves in the jejunal arm to further eliminate this factor, and it seems that food will occasionally enter it otherwise. The time expended, however, to make these valves in a palliative procedure hardly seems justified.

The case in which all but a small portion of the pancreas is removed by a one stage modified Whipple procedure presents several interesting points on which to speculate. From a technical standpoint four modifications are recommended (figs. 1 and 2).

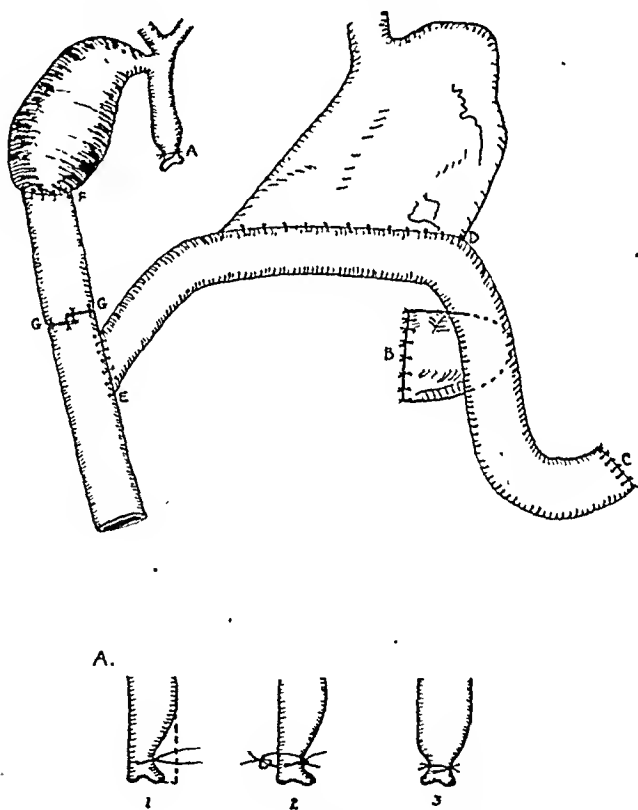


Fig. 2 (case 3).—Completed one stage modified Whipple procedure. A, doubly ligated common duct, with the distal suture transfixed to secure the second suture. B, sutured capsule of the tail of the pancreas. C, sutured blind end of the jejunum. D, anterior Polya antiperistaltic gastrojejunostomy. E, end-to-side jejunojejunostomy. F, cholecystojejunostomy. G, infolding valves to prevent the passage of intestinal contents into the gallbladder.

1. Rather than closure of the end of the stomach and making a posterior gastrojejunostomy, the jejunum is anastomosed side to side to the open end of the stomach. This is time saving.

2. A so-called antiperistaltic anastomosis is made, so that the distal part of the jejunal loop emerges from the lesser curvature of the stomach.

and it is therefore closer to the gallbladder to which it is to be anastomosed. This lessens the pull on the gallbladder resulting from the weight of a long jejunal loop.

3. Anastomosis of the common duct, rather than the gallbladder, to the jejunum has previously been recommended, because of the fatalities which have occurred because the tie on the hugely dilated common duct has slipped or in some way permitted the duct to open. This should not occur if two ties of strong nonabsorbable sutures are used in the following manner: The first tie is transfixed through the wall of the duct with a needle. This suture is tied snugly and the ends temporarily left long. The second tie is not transfixed with a needle but completely surrounds the duct. It is kept in place by tying the remaining long ends of the transfixed ligature around it (fig. 2). This simple procedure, it seems, should prevent fatality from reopening of the ligated end of the common duct. Owing to the proximity of the common duct to the portal vein and hepatic artery, it is technically more difficult to anastomose to the jejunum than is the gallbladder. If the foregoing precaution is taken, it seems that cholecystojejunostomy is preferable to choledochojejunostomy, providing, of course, that the cystic duct is patent.

4. Even when the more desirable Rous principle is utilized in anastomosing the jejunum to the gallbladder, reports suggest that cholecystitis incident to passage of intestinal contents into the gallbladder occasionally occurs. In this case two infolding valves were made in the jejunal arm. This theoretically permits the flow of bile from the gallbladder into the jejunum but hampers the passage of partially digested food upward into the arm beyond the valves. This procedure, it seems, should prevent morbidity from this factor. Warren Cole has recently recommended the placing of two or three valves in the jejunal arm when it is anastomosed at the hilus of the liver following resection of the bile duct because of the extensive stricture.<sup>5</sup>

In the case reported, the patient has presented no symptoms of cholecystitis and is clinically well six months following operation. Evidently a large amount of amylase was liberated into the blood stream after resection of most of the pancreas. This is suggested by a serum amylase level of 800 units on the fifth postoperative day. Three months following operation the serum amylase content was 267 units per hundred cubic centimeters of blood, which is slightly above normal. The pathologic physiology involved is not clear. It is interesting to note that even though only a small portion of the tail of the pancreas remained after operation in this case diabetes did not ensue. The blood sugar content was 73 mg. two weeks after operation, and it is now normal,

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5. Cole, W.: Surg., Gynec. & Obst. 82:104-105, 1946.

six months after operation. Total pancreatectomy in the 8 cases which have been reported is consistently followed by diabetes, which must be carefully controlled by insulin.<sup>4</sup> The patient operated on by Clagett died from a severe reaction to insulin. It therefore seems that total pancreatectomy should not be performed if the sparing of a small portion of the tail of the pancreas does not detract from the realization of an over-all optimum prognosis.

#### SUMMARY

The scope of surgical procedures applicable to the treatment of obstructive neoplasms of the extrahepatic biliary tract is limited. For all practical purposes, individualization of treatment is confined to four methods, namely, (1) local excision, (2) transduodenal resection of the ampulla of Vater, (3) a Whipple type of procedure and (4) palliative shunting of the bile flow.

Four cases are reported which illustrate the indications for each of these procedures.

Four modifications of the Whipple operation are submitted, which it seems decrease operative time, morbidity and mortality rate.

Sparing a small portion of the tail of the pancreas has prevented postoperative diabetes, whereas total pancreatectomy has consistently been followed by diabetes. It is therefore important in resections of the pancreas to leave some pancreatic tissue intact whenever practical.

## HEMODILUTION FOLLOWING EXPERIMENTAL HEMORRHAGE

Influence of Body Movement, of the Ingestion of Water and of Anesthesia Induced  
by Intravenous Administration of Pentothal Sodium

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AND

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**D**ESPITE the large number of studies on hemorrhage, there is little exact information in regard to the phenomenon of hemodilution, this term being used to describe a decrease in the red cell concentration in the blood, as measured by the hematocrit reading, by the erythrocyte count or by the concentration of hemoglobin. While most observers agree that hemodilution (i.e., anemia) ordinarily follows severe hemorrhage, it is generally believed to occur only after the lapse of time. For example, in two textbooks on hematology the hemodilution following a severe hemorrhage is described as follows:

"The red cell count, hemoglobin, and volume of packed red cells, at first misleadingly high as the result of vasoconstriction and of liberation of corpuscles from storehouses such as the spleen, decrease and may continue to fall for several days even though hemorrhage has ceased."<sup>1</sup>

"There will be little or no deviation from normal if an erythrocyte count and hemoglobin determinations are made soon after a hemorrhage . . . . There is a gradual fall . . . during the following hours. This reaches its lowest level after 24 to 72 hours."<sup>2</sup>

Moreover, there is little data as to the factors which influence it. Although hemodilution is presumably a beneficial compensatory mechanism aimed at restoring blood volume, it does so with a protein-poor fluid, which leads to hypoproteinemia. One therefore wonders how decisive a part it plays in the survival from severe hemorrhage.

In the present study, three factors, i. e., body movement, ingestion of water and anesthesia, were studied and found to influence the degree of hemodilution following a single, severe, nonfatal hemorrhage in dogs.

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From the Department of Surgery, Washington University School of Medicine, and Barnes Hospital.

1. Wintrobe, M. M.: *Clinical Hematology*, Philadelphia, Lea & Febiger, 1942, p. 391.

2. Fowler, W. M.: *Hematology*, New York, Paul B. Hoeber, Inc., 1945, p. 160.

## PREVIOUS OBSERVATIONS

Probably the first study of the concentration of red cells following a severe hemorrhage was reported in 1854 by Vierordt.<sup>3</sup> Rabbits and dogs were used without anesthesia and prompt decreases found within a few minutes after bleeding. In two experiments a drop exceeding 50 per cent of the initial value was noted within several hours after the removal in intervals of amounts of blood approximating one fourth to one half of the estimated total circulating blood volume. Although a considerable number of experiments have been reported since then, no attempt to review them will be made. Only a few of the more recent observations will be mentioned under the following headings.

*Anesthesia.*—Experiments reported from this laboratory in 1936 showed that the induction of a general anesthesia with sodium amytal inhibited the hemodilution which occurred in dogs similarly bled under local anesthesia.<sup>4</sup> Three years before this, Adolph, Gerbasi and Lepore<sup>5</sup> compared the effect of ethyl carbamate anesthesia and sodium amytal anesthesia on the red cell concentration following a single hemorrhage of from 20 to 35 cc. per kilogram in 7 dogs. They found an increased concentration of red cells following bleeding in the dogs anesthetized with sodium amytal, not observed in those under anesthesia induced with ethyl carbamate. These authors explained the difference by the discharge of corpuscles from the spleen, which was enlarged and full of blood, due to the effect of sodium amytal, an effect which is not shared by ethyl carbamate. This influence of the barbiturates on the size of the spleen has been observed by others.<sup>6</sup> Of incidental interest is the fact that the aforementioned authors<sup>5</sup> noted that the production of a large store of red cells in the spleen had an apparently beneficial influence inasmuch as dogs anesthetized with sodium amytal withstood more bleedings than those under anesthesia induced with ethyl carbamate. Another observation made by these workers is the fact that the rate of hemodilution was greatly reduced in the absence of the viscera.

In the following studies on hemorrhage, definite differences were observed in hemodilution depending on whether or not a general

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3. Vierordt, K. von V.: Arch. physiol. de heilk. **13**:274, 1854.

4. Elman, R.; Weiner, D. O., and Cole, W. H.: Proc. Soc. Exper. Biol. & Med. **32**:793, 1935.

5. Adolph, E. F.; Gerbasi, M. J., and Lepore, M. J.: Am. J. Physiol. **104**:502, 1933.

6. Bourne, W.; Bruger, M., and Dreyer, N. B.: Surg., Gynec. & Obst. **51**:356, 1930. Essex, H. E., and others: Proc. Soc. Exper. Biol. & Med. **35**:154, 1936.

anesthesia was used. For example, Hirota<sup>7</sup> bled rabbits without anesthesia in amounts up to 50 per cent of the estimated blood volume and demonstrated prompt hemodilution as measured by the hematocrit reading, which fell as much as 52 per cent. This investigator also measured changes in blood and colloidal osmotic pressures and was able to show a relationship between the two, confirming the Bayliss-Starling hypothesis. Thus, when blood pressure was high and colloidal osmotic pressure low, little fluid flowed into the blood stream after hemorrhage, so that restoration of blood volume was slight. On the other hand, when the blood pressure was low and the colloidal osmotic pressure high, restoration of blood volume was pronounced, as shown by a decided hemodilution. Boyd and Stevenson<sup>8</sup> found a drop of 25 per cent in the concentration of hemoglobin within three hours after a single hemorrhage equal to 25 per cent of the estimated blood volume in unanesthetized rabbits. Ikeda<sup>9</sup> removed 15 cc. per kilogram of body weight in unanesthetized rabbits and found that both viscosity and red cell count fell within six to twenty-four hours.

Fine, Fischmann and Frank<sup>10</sup> found that anesthesia induced with pentobarbital sodium had a profound effect on the reaction of dogs to a single large hemorrhage (equal to 30 to 40 per cent of the previously calculated blood volume). These animals invariably went into shock, as compared with complete absence of shock in unanesthetized animals. The latter showed pronounced hemodilution, regaining an average of 53 per cent of the lost blood volume in four hours. Although no data on hemodilution were reported in the anesthetized dogs, it is probable that a failure to restore fluid played an important part inasmuch as it was found that recovery from shock, even when present for one-half hour or more, followed the intravenous injection of isotonic solution of sodium chloride or plasma.

Using pentobarbital sodium anesthesia in dogs, Price, Hanlon, Longmire and Metcalf<sup>11</sup> found little change in the hematocrit reading, even though about 35 cc. per kilogram of body weight was bled and all animals succumbed. Magladery, Solandt and Best<sup>12</sup> bled dogs anesthetized with pentobarbital sodium 18 to 68 per cent of the total blood volume, i. e., until the blood pressure reached 30 mm. of mercury. All but 4 died, 5 at the end of the hemorrhage. In all but 3 cases

7. Hirota, K.: *J. Biochem.* **9**:87, 1928.

8. Boyd, E. M., and Stevenson, J. W.: *J. Biol. Chem.* **122**:147, 1937.

9. Ikeda, T.: *Taiwan Igakkai Zasshi* **41**:322, 1932.

10. Fine, J.; Fischmann, J., and Frank, H. A.: *Surgery* **12**:1, 1942.

11. Price, P. B.; Hanlon, C. R.; Longmire, W. P., and Metcalf, W.: *Bull. Johns Hopkins Hosp.* **69**:327, 1941.

12. Magladery, J. W.; Solandt, D. Y., and Best, C. H.: *Brit. M. J.* **2**:248, 1940.



there was no hemodilution; indeed, in 6 the red cell volume rose between the end of the hemorrhage and death. It is of interest, however, that in only 2 animals was hemodilution found, and these lived the longest (two hours) of those that died. No data on changes in hematocrit reading are recorded on the 4 which recovered. That chloroform probably does not inhibit hemodilution was shown by Chevallier and Trabouyer,<sup>13</sup> who, in dogs so anesthetized, observed hemodilution within five to ten minutes following hemorrhage, which, however, always proved fatal. Using morphine only in dogs, Beard, Wilson, Weinstein and Blalock<sup>14</sup> found no spontaneous change in hematocrit value following removal in intervals of 40 cc. of blood per kilogram of body weight. However, if fluids were injected in similar experiments, the hematocrit level fell.

In 8 cats anesthetized with pentobarbital sodium Brown, Miles, Vaughan and Whitby<sup>15</sup> found a progressive hemodilution following successive bleedings of 5 cc. every ten minutes until death occurred. Hemodilution values were parallel as measured by a fall in hemoglobin concentration, red cell count and hematocrit reading. The final value was between 40 and 50 per cent of the initial value.

Although hemodilution was not studied, it is of interest to mention a detailed study on the effect of various anesthetics on the resistance of dogs to severe hemorrhage, as carried out by Zweifach, Hershey, Rovenstine, Lee and Chambers.<sup>16</sup> An initial bleeding of 20 cc. per kilogram of body weight was followed by 5 cc. every thirty minutes until blood flow ceased in a portion of exteriorized omentum. The least deleterious effects were shown by dogs under local and cyclopropane anesthetics. Thus, in them more blood could be removed (53 and 48 cc. per kilogram) and less collapse occurred at the end of three hours (23 and 33 per cent respectively) as compared with those anesthetized with pentothal sodium and pentobarbital sodium, which withstood but 40 and 30 cc. per kilogram and showed collapse in 100 and 75 per cent at the end of three hours respectively.

*Influence of Fluid Intake.*—That dehydration impairs hemodilution following hemorrhage was demonstrated by Weston, Janota, Levinson

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13. Chevallier, A., and Trabouyer, L.: *Compt. rend. Soc. de biol.* **107**: 1129, 1931.

14. Beard, J. W.; Wilson, H.; Weinstein, B. M., and Blalock, A.: *J. Clin. Investigation* **11**:291, 1932.

15. Brown, G. L.; Miles, J. A. R.; Vaughan, J. M., and Whitby, L. E. H.: *Brit. M. J.* **1**:99, 1942.

16. Zweifach, B. W.; Hershey, S. G.; Rovenstine, E. A.; Lee, R. E., and Chambers, R.: *Surgery* **18**:49, 1945.

and Necheles.<sup>17</sup> In dogs kept without food or water before bleeding, 7 showed a decrease and 8 an increase in the red cell count. By contrast, dogs kept without food but with adequate water before bleeding showed hemodilution in 9 and hemoconcentration in 2. Local anesthesia was used. Calvin<sup>18</sup> noted that dehydration made a striking difference in the degree of hemodilution following a single severe hemorrhage amounting to 25 per cent of the previously calculated blood volume. Dogs deprived of food and water for forty-eight hours previous to hemorrhage exhibited a much smaller drop in hemoglobin content within four hours than similar animals deprived of food but not of water for twenty-four hours previously but given 500 cc. of 0.7 per cent isotonic solution of sodium chloride before bleeding. The type of anesthesia was not mentioned, but was obviously the same in the two groups. In experiments from the laboratory of one of the present authors<sup>19</sup> the ingestion of fluids was shown to increase slightly the ability of dogs to withstand repeated hemorrhage, although no observations were made on its influence on hemodilution.

*The Effect of Position.*—In a communication from this laboratory the immobile position was found to increase the susceptibility of dogs to repeated hemorrhage.<sup>19</sup> No data, however, were made of whether this influence was associated with any difference in hemodilution. Curiously enough, in normal human beings a fall in plasma protein, as much as 0.8 Gm. per hundred cubic centimeters, due to hemodilution, was found during rest in bed.<sup>20</sup>

*Observations Following Hemorrhage in Human Beings.*—Ebert, Stead and Gibson<sup>21</sup> observed a fall in the hemoconcentration for seventy hours in human donors following the removal of 760 to 1,220 cc. of blood. Walsh and Sewell<sup>22</sup> observed progressive hemodilution beginning two hours after bleeding 500 cc. in 6 donors, as measured by a fall in hematocrit value and hemoglobin concentration. Wallace and Sharpey-Schafer<sup>23</sup> studied the changes in hemoglobin concentration in 28 human donors bled 500 to 1,150 cc. and found great individual variations. In only 5 was there any hemodilution within one hour. At some time after bleeding, however, all but 5 showed decreases of 10 to 30 per cent from the initial value. The time of maximum dilution

17. Weston, R. E.; Janota, M.; Levinson, S. O., and Necheles, H.: *Am. J. Physiol.* **138**:450, 1943.

18. Calvin, D. B.: *J. Lab. & Clin. Med.* **26**:1144, 1941.

19. Elman, R., and Davey, H. W.: *Proc. Soc. Exper. Biol. & Med.* **56**:14, 1944.

20. Perera, G. A., and Berliner, R. W.: *J. Clin. Investigation* **22**:25, 1944.

21. Ebert, R. V.; Stead, E. A., and Gibson, J. G.: *Arch. internat. de med.* **68**:1578, 1941.

22. Walsh, R. J., and Sewell, A. K.: *M. J. Australia* **1**:73, 1946.

23. Wallace, J., and Sharpey-Schafer, E. P.: *Lancet* **2**:393, 1941.

in 16 cases occurred within twenty-four hours. Tonkes<sup>24</sup> studied the blood loss following pregnancy and found little hemodilution under three days, whether or not the patients had received isotonic solution of sodium chloride subcutaneously. Browne, Miles, Vaughan and Whitby<sup>15</sup> carefully observed changes in the blood before and at short intervals after bleeding 540 cc. from a donor. The hemoglobin concentration dropped immediately after bleeding, the red cell count one-half hour later and the hematocrit reading not until one and one-half hours later. In a patient estimated to have lost 745 cc. of blood following radical mastectomy, hemodilution was slower in its appearance by several hours but was progressive during four days thereafter.

#### METHODS

Healthy mongrel dogs between 8 and 10 Kg. in body weight were selected. They were maintained on a normal diet for two weeks before experimentation. A single large bleeding was rapidly carried out from the femoral artery, exposed with the animals under local anesthesia by means of a glass cannula introduced into the lumen, through which an amount of blood was removed equaling 40 cc. per kilogram of body weight. The artery was then ligated and the skin closed with sutures.

Hemodilution was measured by changes in the red cell volume, a 1 cc. hematocrit tube being used, into which heparinized blood was placed after its removal from the femoral vein. Preliminary observations had shown that the same hematocrit readings were obtained from arterial as from venous blood. The heparinized blood was spun at 3,000 revolutions per minute for thirty minutes. This was shown to produce the maximum packing of red cells. The initial hematocrit reading before hemorrhage was taken as 100 per cent, and all subsequent readings were calculated as percentages thereof. Samples were removed at one, three, six, ten and twenty-four hours after hemorrhage.

Five groups of experiments were carried out as follows. 1. Five dogs were immobilized in the supine position for ten hours after hemorrhage, during which time nothing was given by mouth. 2. Five dogs were completely mobile and allowed free body movement for ten hours after the hemorrhage but were given nothing by mouth. 3. Five dogs were completely mobile and allowed free movement for ten hours after hemorrhage, during which time water was allowed ad libitum. 4. Four dogs were treated the same as those in group 1 except that pentothal sodium was given for a period of four hours, beginning one hour after hemorrhage and ending five hours after hemorrhage. 5. Five animals were treated the same as those in group 3 except that during a period of one hour, from the third to the fourth after hemorrhage, pentothal sodium was given intravenously. This length of anesthesia failed to influence the hemodilution curve, which was exactly the same as that in group 3.

After the tenth hour all animals were allowed complete movement in the cage and had access to water ad libitum. The amount of water consumed was measured in each instance.

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24. Tonkes, E.: *Zentralbl. f. Gynäk.* 56:2003, 1932.

## EXPERIMENTAL FINDINGS

The findings are recorded in the accompanying two charts. In spite of the considerable variation in individual experiments, the following findings seem clearcut. Full mobility with or without the ingestion of water increases greatly the degree of hemodilution as compared with that of the animals immobilized in the supine position for ten hours. The latter showed some hemodilution during this time, but the

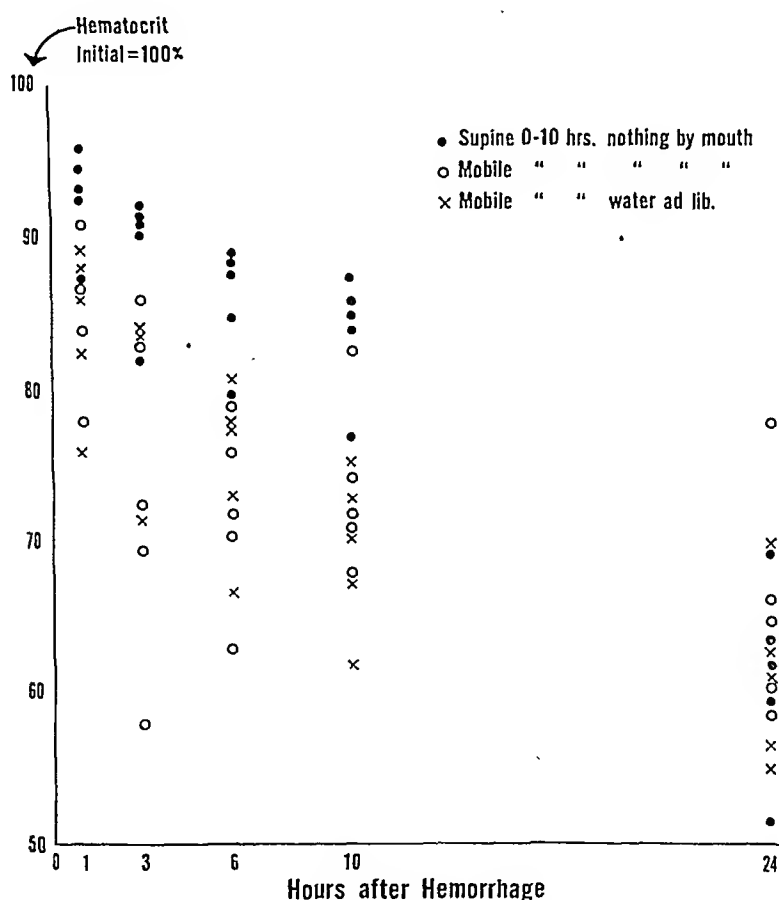


Chart 1.—The effect of mobility and of the ingestion of water. Three groups of 5 dogs each were bled 40 cc. per kilogram of body weight from the femoral artery. Each point represents a hematocrit value. Note that full mobility was followed by the greatest hemodilution. Note also that the hematocrit readings of the mobile dogs allowed nothing by mouth, tended to rise at ten hours, after an early fall. The immobile dogs showed the least hemodilution. Note, however, that, all dogs being allowed full mobility and water ad libitum after ten hours, the hematocrit reading fell to the same level in all groups by the twenty-fourth hour.

hematocrit readings of 4 of the 5 had not fallen below 84 per cent of the initial value, whereas in all but one of the two groups allowed free movement during this period the drop was greater than 75 per cent and in one as low as 62 per cent. In the two groups allowed full

movement, the influence of the ingestion of water is clearly but less strikingly shown. Although the hemodilution up to three and six hours is similar, the red cell volume increased at ten hours in the group of animals given nothing by mouth, thus indicating a reversal of the shift of fluid which entered the blood following the hemorrhage back to the tissues some time between the sixth and tenth hour.

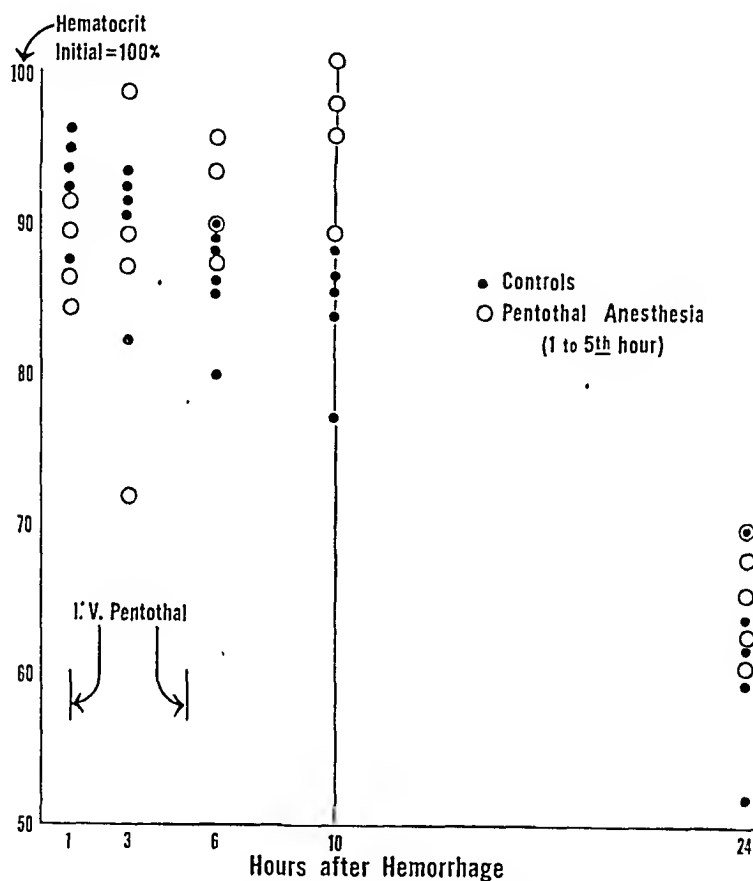


Chart 2.—The influence of pentothal sodium anesthesia. Two groups of 4 dogs each were bled 40 cc. per kilogram of body weight from the femoral artery. Each point represents a hematocrit value. Note the progressive fall in the controls in contrast to the reversal of hemodilution in the anesthetized group, which led at ten hours in 1 case to a value greater than the initial. After ten hours, both groups were allowed full mobility and water ad libitum, the hematocrit value at twenty-four hours being the same in the two groups.

Intravenous administration of pentothal sodium was shown to produce an even greater reversal when given one hour following hemorrhage, at a time when hemodilution had begun. In one experiment the change of fluid shift from the blood to the tissues led to an actual hemoconcentration.

In spite of these variations during the first ten hours, all groups showed the same final degree of hemodilution at twenty-four hours following a period of fourteen hours in which all were allowed full mobility and water *ad libitum*. This confirms previous findings from this laboratory.<sup>25</sup> The total amount of water consumed was similar in all groups, whether it was taken during the entire twenty-four hour period or only during the tenth to twenty-fourth hour. It varied between 70 and 110 cc. per kilogram of body weight, with the exception of 1 dog, who drank only 35 cc. per kilogram of body weight but whose behavior was in no way different from the others.

The amount of pentothal sodium given was sufficient only to keep the animals asleep. It was found at once that this dose was low as compared with that of the unbled animals. For example, in a normal dog it requires at least 25 mg. per kilogram to maintain anesthesia for one hour. After a hemorrhage of 40 cc. per kilogram, but 17 mg. per kilogram is required to maintain the same degree of anesthesia.

Observations were made on the clinical behavior of all animals after hemorrhage. Those kept immobilized in the supine position, when returned to the cages, were definitely prostrated and lay quietly, gradually reviving and partaking of a large amount of water, so that during the subsequent fourteen hours they consumed as much water as animals in the other groups. None of them, however, showed other symptoms, such as vomiting and diarrhea. By contrast, the dogs returned to the cages immediately after hemorrhage were alert and active, but many of them retched and vomited and many defecated, a few repeatedly in small amounts, and occasionally there was liquid stool. These symptoms rapidly subsided, however, within an hour, and after this time few abnormal clinical manifestations were observed. There were no fatalities.

#### COMMENT

Considerable variations were observed in the hemodilution curve of many experiments following a standard hemorrhage, even when all conditions were maintained as constant as possible. Much of this variation is undoubtedly due to differences in the physical condition of the animals in spite of the attempt to select those of uniform size, age and nutrition. Moreover, the susceptibility of dogs to hemorrhage must also depend on the initial blood volume, which varies widely. This is important because body weight is not accurately proportional to blood volume. Had we measured each dog's blood volume and used it as the basis to calculate the dose of blood to be removed, the variations might have been less pronounced. Variations in environmental temperature may be important; however, all the present experiments were

25. Elman, R.; Lischer, C. E., and Wolff, H.: *Am. J. Physiol.* **138**:569, 1943.

done during the spring months, when the indoor air temperature was relatively constant.

In spite of variations, analysis of the graphs presented herewith permits certain definite inferences. Thus, there seems no doubt that the supine, immobile position impairs the ability of fluids to flow into the blood stream, a mechanism which is undoubtedly an attempt to restore the lowered blood volume. Moreover, this impairment is immediately dissipated, even after ten hours of immobility, when the animal is allowed to move about and ingest sufficient water. If the animal is allowed complete movement from the beginning, the influence of the ingestion of water seems of added significance because the progressive hemodilution initially present is not maintained or even reversed when water is withheld.

The influence of position and movement of the body on the fluid shift after hemorrhage may have an important practical bearing when one is considering the advisability of ambulation in patients after injury or operation associated with severe loss of blood. The influence of the ingestion of water is of similar significance. Inferences would depend on whether the best compensated hemorrhage is associated with the greatest degree of hemodilution. On theoretic grounds, the restoration of blood volume by a flow of fluid into the blood would seem to be of obvious compensatory value. Unfortunately, this fluid is free not only of red cells but also of plasma protein. It is interesting, therefore, to speculate as to whether the anemia and hypoproteinemia produced by hemodilution may not do more harm than good, especially when it is pronounced.

From the observations of others, as already cited, hemodilution in general was associated with a more favorable outcome. Experiments are now under way in the attempt to add further data on the exact relationship between the degree of hemodilution and the mortality rate. In a few experiments in which death followed a simple, severe hemorrhage, we have already noted a conspicuous terminal change from hemodilution to hemoconcentration.

The influence of intravenous administration of pentothal sodium in producing hemoconcentration after the initial hemodilution seems striking and unequivocal. If hemodilution is looked on as a beneficial compensatory mechanism, obviously pentothal sodium must be considered as exerting a deleterious influence. With one possible exception<sup>5</sup> most of the observers in experiments already described found that the administration of barbiturates is deleterious during hemorrhage. Pentothal sodium obviously has a profound influence on the movement of fluids after hemorrhage; further study is certainly indicated in view of the widespread use of this agent.

## CONCLUSIONS

Hemodilution promptly appeared within one hour, and it persisted up to twenty-four hours following a single, severe (40 cc. per kilogram), nonfatal hemorrhage produced under local anesthesia in dogs. The greatest degree of hemodilution occurred when full mobility and free access to water were allowed immediately after hemorrhage. Immobility in the supine position inhibited the degree of hemodilution. The withholding of water during full mobility tended to change hemodilution to hemoconcentration.

Pentothal sodium given intravenously after the start of posthemorrhagic hemodilution reversed the process and even led to actual hemoconcentration. After hemorrhage, dogs require a much smaller dose of pentothal sodium to maintain anesthesia.



## TRAUMATIC AND AMPUTATION NEUROMAS

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THE CAUSE of painful and traumatic neuromas is not clearly understood. The investigation reported in this paper has been undertaken with the hope of determining whether or not the various methods of dealing with the divided nerve ends influence their occurrence or prevention. The records of the Laboratory of Surgical Pathology have been examined for proved cases, and these as well as amputations of major extremities in the Presbyterian Hospital from 1932 to 1945 were reviewed. Only records with adequate follow-up were used.

### DEFINITION

After section, the distal end of the nerve may enlarge and simulate a tumor. These enlargements, called neuromas, are not true neoplasms. The nodule is made up of granulation tissue through which many strands of regenerated or proliferated axons with Schwann sheaths pass. These are arranged in interlacing bundles running in all directions. It is believed that the granulation tissue preceding neuroma formation arises from the blood vessels of the endoneurium and perineurium of the involved nerve as well as from the adjacent soft tissues.

### REVIEW OF CASES

*Traumatic Neuromas.*—An analysis of these records showed that there were sixty-two neuromas following trauma in 61 patients. Pain was the most prominent symptom in 41 cases, anesthesia in 24 and paralysis in 17. Most patients had several complaints. There were 36 men and 25 women.

The fourth decade had the greatest incidence, with 16 cases, and the third decade ranked next, with 15; the older groups had fewer cases. Thus, 50 per cent of the neuromas in this group occurred in the third and fourth decades, corresponding to the period of greatest exposure to industrial hazards. This study includes 56 white, 4 Negro and 1 Chinese patient. Symptoms existed from two months to more than twenty years.

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The common exciting factor in these cases of neuroma was trauma. A frequent story was that the patient pushed his hand through a window or fell on a broken bottle and cut his wrist. Industrial hazards associated with punch presses, stamping machines and choppers are common causes. Frequently an incomplete examination of the extremity resulted in the failure to recognize neural injury. In some, the injury was discovered but an inadequate surgical repair was performed. Thirty cases occurred in the two mentioned groups. In 15 the neuroma followed amputation. These will be discussed separately. In 9 the neuroma occurred after fractures, in 6 after compound fractures, in 2 after the simple type with open reduction and in 1 after a simple type with closed reduction. Mastoidectomy, thyroglossal cystectomy, cholecystectomy, radical mastectomy and other operations each preceded the neuroma in 1 or 2 cases.

Treatment consisted, first, in a detailed examination of the patient's disability and the determination of the nerve or branches involved. The location of a point of maximum tenderness was marked on a diagram, the wound was then explored, the neuroma excised and a neurolysis and neurorrhaphy performed. Fine silk sutures through the epineurium or perineurium were used to maintain the anastomosis. Often, a tenolysis and tenorrhaphy of the adjacent tendons was performed. A plaster cast or splint was utilized as external immobilization to hold the repaired structures in position.

Of the sixty-one neuromas, forty-six followed trauma and fifteen followed amputation. Of the forty-six following trauma, four showed excellent results, with recovery of full sensation and full motion without pain. Twenty-seven patients had a good result, with improved sensation and motion and no pain. Four had a fair result, with improved sensation, motion and some pain. In 2 cases there was little or no improvement. There were no recurrences. Nine cases could not be followed.

Of the 15 cases of neuroma following amputation, results of excision were good in 7, fair in 3 and poor in 3, and 2 patients died soon after the operation of intercurrent disease. Four of the neuromas occurred after amputations of fingers, leaving eleven which occurred after amputations of a major extremity. Three of these were performed in this hospital and the others elsewhere.

*Neuromas After Amputation.*—From 1932 to 1945, there were 67 patients who had eighty-six amputations. The patients dying soon after operation are not included. There were 45 men and 22 women who had amputations. The highest incidence of amputations occurred in the sixth, fifth and seventh decades, in that order. This series includes a large number of patients whose extremities were amputated for vascular disease or infection following vascular trauma.

Amputation was performed for arteriosclerotic gangrene in 30 cases, neoplasm in 12, arteriosclerotic gangrene with diabetes in 11, compound fractures in 9, thromboangiitis obliterans in 8 and embolism in 6. Seven amputations were done for uncontrollable ascending infection, two for neurotrophic ulcers, one for ruptured iliac aneurysm, with resulting gangrene of the lower extremity, and one for progressive myositis ossificans.

The amputations were done by or under the supervision of seventeen attending surgeons. Local infiltration or spinal or general anesthesia was used, depending on the patient's condition. Refrigeration was used in 2 instances.

In this analysis, all the nerves cut at the same level are recorded as if they were one nerve. Thus, for example, in amputation of a single leg, the peroneal, anterior tibial and posterior tibial nerves have been considered as a unit.

These nerves in different cases were treated by various technics. Into some procaine hydrochloride was injected and they were ligated and transected at the same or higher levels; into others procaine hydrochloride and alcohol was injected, and they were ligated and then divided. Some were transected and received no other treatment. Others were transected and ligated. In the true guillotine amputation only transection was done. Injection of procaine hydrochloride prior to section was done thirty-two times in connection with some other procedure. Injection of alcohol was used fifty-three times. In 50 cases, the nerve was isolated, pulled down, ligated, sectioned and then allowed to retract to a higher level.

Fifty-four amputations gave good results, with a well healed stump and no pain or tenderness. Fair results were obtained in 15 cases and poor results in 17 cases, because of painful or unhealed stumps. Three neuromas occurred in eighty-six amputations done in this hospital. Each of these occurred in patients who had a true guillotine amputation for ascending infection in which the nerve was only transected at the same level. In these cases, wound healing was facilitated by skin traction or skin grafting. In other cases of true guillotine amputation, a revision or reamputation of the stump was performed, the nerve was ligated and sectioned at a higher level and no neuromas resulted. In cases in which neuromas were removed at this hospital after amputation elsewhere, a history of guillotine amputation or infection was elicited. In our 3 cases, the amputation neuroma was excised at a higher level, the nerve was placed in normal soft tissues and no further neuroma resulted.

#### COMMENT

*Traumatic Neuromas.*—The experience at the Presbyterian Hospital with neuromas after trauma is in agreement with the experiences elsewhere. The importance of a careful examination of a patient who

has an injury in the vicinity of a nerve cannot be overemphasized. Even if the point of entry of a sharp instrument is not immediately over the nerve, a careful local neurologic examination of both the sensory and the motor components should be done. This has been stressed by Stoney,<sup>1</sup> Coleman,<sup>2</sup> Spurling<sup>3</sup> and others. The theories and mechanisms in nerve healing, regeneration and formation of neuromas were described by Gurdjian and Smathers,<sup>4</sup> Weiss,<sup>5</sup> Davis and Hiller<sup>6</sup> and others.

As soon after the injury as possible, the severed nerve ends should be debrided and sutured together end to end, either fine silk or tantalum wire sutures being used. If there is an absence of nerve tissue, prohibiting primary anastomosis, the nerve should be mobilized by dissecting up the extremity, so that by flexion of the adjoining joints the nerve ends may be approximated. The extremity should then be held in position by some means of external immobilization.

If a primary repair is impossible within approximately six hours, ten to fourteen weeks should be allowed to elapse before neuroorrhaphy. Electric stimulation of the muscles which are normally innervated by the injured nerve must be used to preserve normal muscle tone and contractility. The use of tantalum and other inert suture material may decrease the occurrence of granulation tissue, which aids in the formation of a neuroma.

The neuroma, once formed, should be dissected from the surrounding tissues and excised in slices proximally and distally until normal nerve fasciculi are seen. The nerve ends should then be sutured and, if possible, placed in a new area of soft tissue. A transplant of fat or tantalum foil around the site of anastomosis may prevent adhesions.

*Neuromas After Amputation.*—The most interesting group of neuromas gathered in this series is that in which the growth occurred after amputation. Fifteen cases were found in this group. Three of these followed amputations in this hospital and occurred after a true guillotine amputation. After this procedure, stump closure may be

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1. Stoney, R. A.: Forty Years' Experience with Nerve Suture, Irish J. M. Sc., March 1944, pp. 85-92.

2. Coleman, C. C.: Peripheral Nerve Surgery: Diagnostic Considerations, J. Neurosurg. 1:123-132 (March) 1944.

3. Spurling, R. G.: Symposium on War Surgery: Use of Tantalum Wire and Foil in Repair, S. Clin. North America 23:1491-1504 (Dec.) 1943; Nerve Surgery: Technical Considerations, J. Neurosurg. 1:133-138 (March) 1944.

4. Gurdjian, E. S., and Smathers, H. M.: Peripheral Nerve Injury in Fractures and Dislocations of Long Bones, J. Neurosurg. 2:202-219 (May) 1945.

5. Weiss, P.: Sutureless Reunion of Severed Nerves with Elastic Cuffs of Tantalum, J. Neurosurg. 1:219-225 (May) 1944; Technology of Nerve Regeneration, *ibid.* 1:400-450 (Nov.) 1944.

6. Davis, L., and Hiller, F.: Regeneration in End to End Suture, Grafts, and Gunshot Injuries, Tr. Am. Neurol. A. 70:178-179, 1944.

aided by traction on the skin or by skin grafting and the stump later revised in such a way that the nerve lies at a level higher than the scar.

A study of the neuromas removed in this hospital after amputations elsewhere showed that they resulted from similar causes. In most guillotine amputations performed at this hospital, the wound was allowed to heal assisted by skin traction or grafts, and later the stump was revised. No neuromas occurred in this revised group. Thus, it seems that neuromas and tender stumps arise oftener after a true guillotine amputation or when infection is present or develops soon after the procedure in such a way that the nerve is included in the scar tissue. This does not happen in the so-called modified guillotine amputation used at this hospital (Smith<sup>7</sup>).

The symptoms of these neuromas are characteristic. They are produced by pressure, irritation of the area or movement of the scar tissue and are described as radiating down the former distribution of the nerve often being relieved by the local infiltration of procaine hydrochloride. White<sup>8</sup> suggests that the pain may be due to stimuli from the neuroma or from the sensory areas of the cerebral cortex. Repeated ill advised surgical procedures to rid the patient of his complaints may intensify rather than alleviate the symptoms. Spurling<sup>9</sup> and Boldrey<sup>9</sup> list the harmful and the advised methods of treatment.

The phantom limb syndrome occurred in only 3 patients with amputations. Of these, not one had a palpable neuroma.

This review suggests that the treatment of nerve ends is of importance in the prevention of a neuroma. The nerve should not be allowed to be included in the scar tissue which follows the operation. Following the technics used in the Presbyterian Hospital, there were only three neuromas. A review of the literature suggests that injection of alcohol into the nerve is harmful rather than helpful. Experimental work of Huber and Lewis showed delay in the regeneration of nerve fibers after injection of alcohol, but other reports have not shown a significant decrease in the frequency or size of neuromas or decrease in the pain or incidence of the phantom limb with this procedure alone. Livingston<sup>10</sup> and Bate<sup>11</sup> do not favor injection of alcohol.

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7. Smith, B. C.: Amputation Through Lower Third of Leg for Diabetic and Arteriosclerotic Gangrene, *Arch. Surg.* **27**:267-295 (Aug.) 1933.

8. White, J. C.: Pain After Amputation (Especially Due to Neuroma and Phantom Limb) and Its Treatment, *J. A. M. A.* **124**:1030-1035 (April 8) 1944.

9. Boldrey, E.: Amputation Neuroma in Nerves Implanted in Bone, *Ann. Surg.* **118**:1052-1057 (Dec.) 1943.

10. Livingston, K. E.: Phantom Limb Syndrome: Discussion of Role of Major Peripheral Nerve Neuromas, *J. Neurosurg.* **2**:251-255 (May) 1945.

11. Bate, J. T.: Method of Treating Nerve Ends in Amputation Stumps, *Am. J. Surg.* **64**:373-374 (June) 1944.

There are numerous ways of treating nerve ends. Boldrey<sup>9</sup> reviewed the older methods and suggested one of his own. Herrmann and Gibbs,<sup>12</sup> Weiss,<sup>5</sup> Spurling,<sup>3</sup> Poth<sup>13</sup> and others have suggested various treatments of nerve ends to prevent neuromas.

This study suggests that the best method of preventing a neuroma after amputation is the isolation of the nerve from the surrounding tissue, the nerve being gently pulled down so as to permit retraction into normal soft parts, and ligation with some nonabsorbable material such as silk or tantalum wire. The ligature should be placed with enough tension to prevent bleeding but not to cut through the perineurium. The nerve should be sectioned below the ligature and allowed to retract into the soft tissues without necessarily injecting anything into the nerve.

#### CONCLUSIONS AND SUMMARY

1. The cases of traumatic neuromas from the records of the Presbyterian Hospital, New York, are reviewed. The commonest causes of neuromas of this type are either failure of the examining physician to recognize a nerve injury or else a poor reparative procedure.

2. The amputations done on major extremities are also reviewed. In eighty-six amputations done at the Presbyterian Hospital only three neuromas occurred.

3. The occurrence of the neuroma seems to be associated with infection or inclusion of the nerve in scar tissue. Tender stumps and neuromas occur less frequently when a reamputation or revision of the stump is carried out.

4. The best method of prevention at present seems to be ligation and section of the nerve as high as possible above the level of amputation, so that the nerve end is embedded in soft tissue and not in dense scar tissue. Nothing need be injected into the nerve with the idea of prevention of growth.

Dr. Beverly C. Smith assisted in the preparation of this paper.

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12. Herrmann, L. G., and Gibbs, E. W.: Phantom Limb Pain: Relation to Treatment of Large Nerves at Time of Amputation, *Am. J. Surg.* **67**:168-180 (Feb.) 1945.

13. Poth, E. J., and Fernandez, E. B.: Prevention of Neuroma Formation by Encasement of the Severed Nerve End in Rigid Tubes, *Proc. Soc. Exper. Biol. & Med.* **56**:7-8 (May) 1944. Poth, E. J.; Fernandez, E. B., and Drager, G. A.: Prevention of Formation of End-Bulb Neuromata, *ibid.* **60**:200-207 (Nov.) 1945.

# AIR IN THE BILIARY PASSAGES

A Review and Report of a Case

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OUR BELIEF is that the future success in the diagnosis of internal biliary fistula lies not in roentgenologic examination exclusively but more in evaluation of the pathologic antecedents that accompany the biliary fistula. With more emphasis placed on clinical study of cases of biliary disease, a greater number of biliary fistulas will be recognized earlier, thus minimizing future complications, and with more attention to the preoperative care the present mortality rate following operations on internal biliary fistulas will be reduced.

Spontaneous internal biliary fistulas are infrequent. The majority result from infections and calculi in the gallbladder or are caused by a perforative ulcer or a malignant growth of the stomach or bowel. According to the literature, in only 108 cases have internal biliary fistulas been recognized preoperatively, and all have been diagnosed by roentgenologic examination. Of this number, including our case, in only 12 cases has diagnosis been made by visualization of air or gas alone in the biliary passages.

The diagnosis of this type of fistula and the high death rate the fistula carries are the most important features of any discussion on internal biliary fistula. Because of certain characteristics all fistulas possess, as pointed out in the paper, in only a small percentage of cases will the roentgenologic examination be of any value in the diagnosis. A review of the literature indicates that little thought has been given to the value of presumptive diagnosis based on pathologic antecedents, which may include elimination of a large stone by the bowel, acute paralytic ileus or spontaneous diarrhea occurring during a well defined biliary colicky attack, chronic diarrhea associated with frank biliary symptoms, attacks of pain of biliary nature followed with chills and fever and low grade jaundice or acute intestinal obstruction caused by impaction of a large gallstone in the lower end of the ileum.

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Some of the biliary antecedents are of major importance, especially passage by the rectum of a gallstone of such size that it could not have escaped the normal route by the ampulla and the chronic diarrhea associated with typical biliary symptoms. On a presumptive diagnostic basis the patient in our reported case presented several pathologic antecedents: spontaneous diarrhea, which occurred at the time of the development of the fistula, and acute biliary colicky attacks of pain followed by chills, fever and jaundice.

#### INCIDENCE

There appears to have been considerable variation in the incidence of internal biliary fistulas in different periods. During the nineteenth century, Courvossier<sup>1</sup> and other writers on this subject found a greater incidence than has been reported during the past three decades. Roth,<sup>2</sup> of Basel, Switzerland, sectioned 166 patients who had died from gallstones during the nine year period from 1872 to 1881, and in this number he found 14 patients who had had either recent or old perforations of the gallbladder or bile ducts. Courvossier reported an incidence of 4.8 per cent of biliary fistulas at autopsies of patients who died from gallbladder disease during the six year period from 1882 to 1888. Only rarely was a correct diagnosis of internal biliary fistula made during life; hence the lack of proper treatment probably accounts for the high death and autopsy rates at this early period. In the past three decades the reported incidence of internal biliary fistulas has been lower. For the twenty-four year period from 1915 to 1939, Dean<sup>3</sup> found only 1.2 per cent of chronic infections of the gallbladder to be complicated by internal biliary fistulas. Puestow<sup>4</sup> reported finding 16 cases of internal biliary fistulas in five hundred operations for benign disease of the biliary tract, an incidence of 3.2 per cent. This smaller incidence of internal biliary fistulas in recent decades is probably the result of earlier diagnosis and improved methods of surgical treatment of chronic disease of the gallbladder.

#### ETIOLOGY

Infection and calculi in the biliary tracts are responsible for production of the greatest number of internal biliary fistulas.

The inflammatory process in the biliary system results in formation of adhesions between the involved viscus and neighboring organs. Because of the anatomic position, the frequency of involvement is in the following order: duodenum, colon and stomach. Pressure from a

1. Courvossier, L. G.: *Casuistisch-statistische Beiträge zur Pathologie und Chirurgie der Gallenwege*, Leipzig, F. C. W. Vogel, 1890, pp. 83-114.

2. Roth, cited by Courvossier.<sup>1</sup>

3. Dean, G. O.: *Internal Biliary Fistulas*, *Surgery* 5:857-864 (June) 1939.

4. Puestow, C. B.: *Spontaneous Internal Biliary Fistula*, *Ann. Surg.* 115: 1043-1054 (June) 1942.



stone against the inflamed wall of the gallbladder produces erosion and necrosis and leads to perforation. This may then result in one of the following conditions: the formation of a walled-off fistula between the gallbladder and the other involved viscus, with spilling of septic gallbladder contents into the bowel; formation of a pericholecystic abscess, or perforation into the free peritoneal cavity, with the development of generalized peritonitis.

Other less common causes of internal biliary fistula are perforated duodenal ulcer, neoplasms of the stomach or gallbladder and hydatid infestation.

Pataro,<sup>5</sup> Garland and Brown<sup>6</sup> and others stated that when the fistula is between the common duct and the duodenum it is almost always the result of a perforated duodenal ulcer. Murchison,<sup>7</sup> working before the days of roentgenologic examinations, expressed the opinion that fistulas between the gallbladder and the colon usually resulted from malignant growths, whereas Stevenson and Sherwood<sup>8</sup> reported in 1940 that in 5 such cases in which diagnosis was made roentgenologically in this country, all were the result of infection and calculi. There is disagreement as to whether chronic phlegmonous cholecystitis without stones may produce a fistula.

#### PATHOLOGY

The pathologic changes of internal biliary fistula consist of extensive adhesions involving the bowel, gallbladder and liver. The gallbladder is contracted, thickened and fibrotic and may or may not show additional stones. The cystic duct is usually open and may be enlarged. The common duct is frequently blocked in its lower end by a stone, with resultant dilatation of the common and hepatic ducts and biliary radicles. Hepatitis may result from spread of intestinal contents through the fistula and biliary system into the hepatic substance. The fistulous tract itself may vary in size and may remain patent or become closed.

Intestinal obstruction may occur when a large stone becomes impacted in the terminal ileum or when a paralytic ileus results from periduodenal inflammation. The inflammatory type of obstruction usually occurs during development of the fistula as a result of one of the fol-

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6. Garland, L. H., and Brown, J. M.: Roentgen Diagnosis of Spontaneous Internal Biliary Fistulae, Especially Those Involving the Common Bile Duct, *Radiology* 38:154-159 (Feb.) 1942.

7. Murchison, C.: A Clinical Lecture on Diseases of the Liver, Jaundice and Abdominal Dropsy, edited by T. L. Brunton, London, Longmans, Green & Co., 1885, p. 569.

8. Stevenson, C. A., and Sherwood, M. W.: The Roentgen Diagnosis of Cholecystocolic Fistula, *Radiology* 35:616-621 (Nov.) 1940.

lowing mechanisms: paralytic ileus due to local peritonitis; volvulus of the small bowel induced by the violence of the gallstone colic; reflex spasm secondary to the passage of the stone through the newly formed fistulous tract, or a result of adhesions. This type of obstruction is more commonly seen when the fistula is of the biliary-duodenal type. Four cases of inflammatory obstruction of this type have been reported by Bengolea and Suárez.<sup>9</sup>

#### CLINICAL MANIFESTATIONS

The clinical manifestations of internal biliary fistula are similar to those usually seen in chronic biliary disease, except that they are severer. Colicky pains, jaundice, chills and fever are the signs oftenest seen. Frequently there is obstruction of the common bile duct with the symptoms usually related to such obstruction. Diarrhea probably occurs more frequently in spontaneous internal biliary fistula than has been reported in the literature. When diarrhea occurs in association with other symptoms of biliary disease, the existence of a biliary fistula should be suspected. An acute or sporadic form of diarrhea may occur in cholecystoduodenal fistula and is believed to be secondary to the sudden spilling of the septic contents of the gallbladder into the intestine at the time of fistulous formation. A chronic form of diarrhea may occur in the cholecystocolic type of fistula, in which the bile reaches the colon in an unoxidized form and produces a hyperperistalsis by its irritant effect on the mucosa of the colon. Intestinal obstruction has been mentioned before; its presence in a patient with symptoms or history of biliary disease should arouse suspicion that a biliary fistula has formed.

Many internal biliary fistulas are asymptomatic owing to the fact that they remain open to provide adequate drainage. Oftener the fistula contracts because of inflammation and fibrosis, resulting in a return of the symptoms of obstruction of the common duct, namely, chills, fever and jaundice. It has often been asserted that formation of a fistula is nature's cure for an obstruction of the common bile duct. However, the other features connected with formation of a fistula, such as the complications mentioned and the high mortality rate associated with surgical cure, would seem to make the "cure" worse than the disease.

#### ROENTGENOLOGY

With improvement in roentgenologic diagnosis and increase in the number of patients having roentgenologic studies made for gallbladder and other gastrointestinal complaints, more likely a greater number of internal biliary fistulas will be recognized by roentgenologic examination in the future. More fistulas are not recognized by roentgenologic

9. Bengolea, A. J., and Velasco Suárez, C.: Las fistulas bilares internas; contribucion a su estudio, *Rev. med.-quir. de pat. fem.* 7:125, 1936.

examination because in biliary fistulas, as in other fistulas, after the immediate spill of the retained secretions and the back pressure of the blocked channels have been taken care of by formation of the fistula, the fistula in a short time will begin to contract from the inflammation and fibrosis. The life of a fistula in its original size is short. The activity of the fistula will depend largely on retained stones or formation of new stones in the gallbladder and the degree of blockage of the common duct. Consequently, fistulas of large size and recent development will more likely permit the influx of the barium sulfate into the biliary tree during a roentgenologic study after a meal of barium sulfate than a fistula of long duration which has become fibrosed. The visualization of air or gas in the biliary tree is due not so much to size of the fistula as to infection in the biliary tree.

Garland and Brown reported that in 1942 they found 85 cases of spontaneous internal biliary fistulas recorded as having been diagnosed by roentgenologic examination. With this number they reported 5 additional cases. Of this series of 90 cases of internal biliary fistula, in only 9 cases was the presence of air or gas alone revealed in the biliary passage. Of the remainder of the cases, in 76 diagnosis was made by influx of barium sulfate and in the other 5 cases diagnosis was made by both influx of barium sulfate and visualization of air.

From 1941 through 1944, there were 17 cases of internal biliary fistulas diagnosed roentgenologically and recorded. In only 2 of these cases was air or gas alone revealed in the biliary ducts and hepatic radicles. In 2 other cases both influx of barium sulfate and visualization of air were revealed. In the remainder of cases only influx of barium sulfate was revealed.

In this last review of reported cases, the 14 cases of acute intestinal obstruction, caused by impaction of a gallstone, as reported by Rigler, Borman and Noble<sup>10</sup> were not included. They declared that roentgenologic study of the abdomen revealed the presence of air or gas or the influx of barium sulfate in the biliary tree in all cases except 1. The reason for omitting these 14 cases was that their point of discussion was directed primarily toward the acute intestinal obstruction resulting from gallstone impaction and not to the fistula itself, as the findings were merely coincidental. Obviously, the general impression is that if a gallstone has attained size sufficient to block the lumen of the small bowel, it will rarely make its escape through the normal route by the ampullae but instead will escape into the bowel through a fistulous tract originating in the gallbladder or one of the bile ducts.

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10. Rigler, L. G.; Borman, C. N., and Noble, J. F.: Gallstone Obstruction: Pathogenesis and Roentgen Manifestations, *J. A. M. A.* **117**:1753-1759 (Nov. 22) 1941.

The table gives the number of cases of internal biliary fistulas diagnosed by roentgenologic examination, the number of cases which revealed presence of air or influx of barium sulfate into the biliary passages and the name of the author.

## MORTALITY

The mortality rate following operation for spontaneous internal biliary fistula is greater than that seen in operations for chronic benign cholecystic diseases. In the latter group of uncomplicated cases, rarely will

*Use of Air or Barium in Diagnosis of Biliary Fistula.*

| Year | Author  | Cases | Air or Barium Sulfate  |
|------|---|-------|--|
| 1942 | From survey of literature made by Garland and Brown <sup>6</sup>          | 85    | Air: 9 cases<br>Barium sulfate: 76 cases   |
| 1942 | Garland and Brown <sup>6</sup> .....                                      | 5     | Failed to state how many of the cases revealed air or influx of barium sulfate into the biliary passages     |
| 1941 | Eliason and Stevens <sup>11</sup> .....                                   | 1     | Clinical finding based on chronic biliary disease complicated by acute intestinal obstruction from gallstone |
| 1941 | Rigler, Bormann and Noble <sup>10</sup> .....                             | 14    | Failed to state how many of the cases revealed air or influx of barium sulfate into the biliary passages     |
| 1942 | Tracey, M. L., and McKell, D. M., Jr.: S Clin North America 23: 717, 1943 | 5     | Air: 1 case<br>Barium sulfate: 4 cases   |
| 1942 | Puestow, O. B.: Ann. Surg. 115: 1043, 1942                                | 2     | Barium sulfate   |
| 1942 | Deinao, P. J.: Am. J. Roentgenol. 47: 298, 1942                           | 1     | Barium sulfate   |
| 1942 | Taylor, W. B.: Canad. M. A. J. 47: 332, 1942                              | 2     | Barium sulfate   |
| 1943 | Santora, P. J.: Radiology 41: 74, 1943...                                 | 1     | Barium sulfate   |
| 1943 | Pataro <sup>5</sup> .....   | 2     | Air: 1 case<br>Barium sulfate: 1 case  |
| 1944 | Slinger, A.: Rev. Gastroenterol. 11: 409, 1944                            | 1     | Barium sulfate   |
| 1944 | Brandel, E.: Acta radiol. 25: 333, 1944...                                | 2     | Air: 1 case<br>Barium sulfate: 1 case  |
| 1946 | Donald, Meadows and Silbermann.....                                       | 1     | Air  |

the surgical mortality rate exceed 1 to 3 per cent, whereas in operations for internal biliary fistula the mortality rate often reaches an alarmingly high figure. Dean reports a mortality rate of 52 per cent. He stated that out of 25 patients with internal biliary fistula operated on 13 patients died after operation. Eliason and Stevens,<sup>11</sup> reporting from a smaller series, stated that 3 of the 5 patients with internal biliary fistula operated on died, yielding a mortality rate of 60 per cent.

11. Eliason, E. L., and Stevens, L. W.: Spontaneous Internal Biliary Fistula, Am. J. Surg. 51:387-392 (Feb.) 1941.

There are several factors responsible for the high death rate following operation for cure of internal biliary fistula: 1. The age incidence in which internal biliary fistulas are most frequently seen is important. Judd and Burden,<sup>12</sup> after a survey of 153 cases of internal biliary fistula, found the average age to be in the sixth decade. Many patients at this age will present evidence of degenerative changes in the cardiovascular and renal organs, which, if present, will likely influence the surgical picture following any major operation. 2. The type of pathologic condition which is responsible for formation of the fistula is an important factor. It is true that the greater number of internal biliary fistulas result from infections and trauma of the calculi, but there is a small group of cases in which the fistula follows a perforation of a carcinoma of the gallbladder or stomach. In either location in which the carcinoma is present and fistula develops, any operative procedure instituted for correction of the fistula or cure of the malignant growth is followed by a high death rate. 3. Other factors are the local changes in tissue occurring at the site of the fistula, which may encourage operative complications, and, too, the hepatic damage in the form of hepatitis which the fistula produces from escape of the intestinal contents into the bile ducts and biliary radicles. These last two conditions probably are the greatest factors in the high mortality rate seen in operations for internal biliary fistula. Finally, because of present day methods of diagnosis, which is chiefly by roentgenologic examination, only a small percentage of internal biliary fistulas are recognized preoperatively, and as a result the majority of these patients do not receive adequate preoperative care and are not able to meet the demand that a prolonged technical operative procedure for the cure of internal biliary fistula requires (hence, desire for preoperative diagnosis).

#### TREATMENT

The surgical treatment of internal biliary fistula is much more difficult than that of ordinary biliary disease. The gallbladder, biliary ducts, fistula and intestine are all usually surrounded by a mass of adhesions. The gallbladder is usually found contracted and fibrotic and contains necrotic material. The bowel wall around the fistula is indurated and fibrotic, and, after removal of the fistulous stoma, the lumen of the bowel may be so small as to threaten obstruction and require a gastroenterostomy. Even after the fistula is successfully removed and the opening of the bowel is closed, there still remains the problem of dealing with an obstructed and dilated common bile duct. Obviously, cases in which conditions are diagnosed preoperatively and in which patients can be properly prepared for such extensive operation will be followed by

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12. Judd, E. S., and Burden, V. G.: Internal Biliary Fistula, *Ann. Surg.* **81**: 305-312 (Jan.) 1925.

a lower mortality rate than those in which the fistula is found for the first time on the operating table.

#### REPORT OF A CASE

The patient was a 52 year old white man, a railroad worker, who had had periodic attacks of acute pain and soreness in the right upper quadrant of the abdomen, accompanied with vomiting, chills and fever, jaundice and diarrhea. The first attack occurred thirteen years before admission and lasted about three weeks. He was relatively symptom free for five years, after which he had a

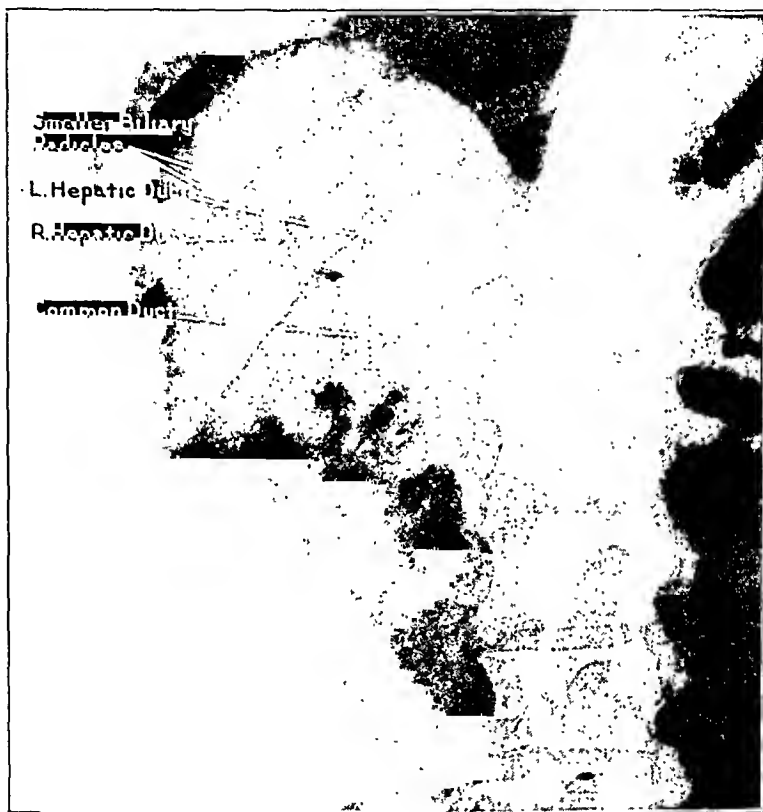


Fig. 1.—Following ingestion of dye (priodax), the roentgenogram revealed a nonfunctioning gallbladder and air in the common and hepatic ducts and biliary radicles.

second attack similar to the first, except for absence of diarrhea. During the next eight years he had several more attacks. During the last six months previous to admission, the attacks came so frequently that he hardly recovered from one before another one began. For approximately eight years before admission he had been under treatment for diabetes mellitus. This had been adequately controlled by diet and protamine zinc insulin. At the time of admission, he had been suffering about two weeks from his latest attack. He had low grade jaundice, a septic type of temperature and a moderate amount of pain in the right upper quadrant of the abdomen. The stools were normal in color, and physical exami-

nation was noncontributory except for tenderness and moderate rigidity in the right upper quadrant, moderate jaundice and absence of the right leg at the mid-thigh (following amputation for a complicated fracture).

Laboratory data were as follows: hemoglobin content, 9 Gm. (58 per cent); red blood cells, 3,790,000 per cubic millimeter; white blood cells, 9,400 per cubic millimeter, and segmented cells, 78 per cent.

Studies of blood chemistry showed a sugar content of 130 mg. per hundred cubic centimeters, serum protein content of 7 per cent and icterus index of 15 per cent. The urine was amber colored, with a specific gravity of 1.026. There were many pus cells and an occasional red blood cell.

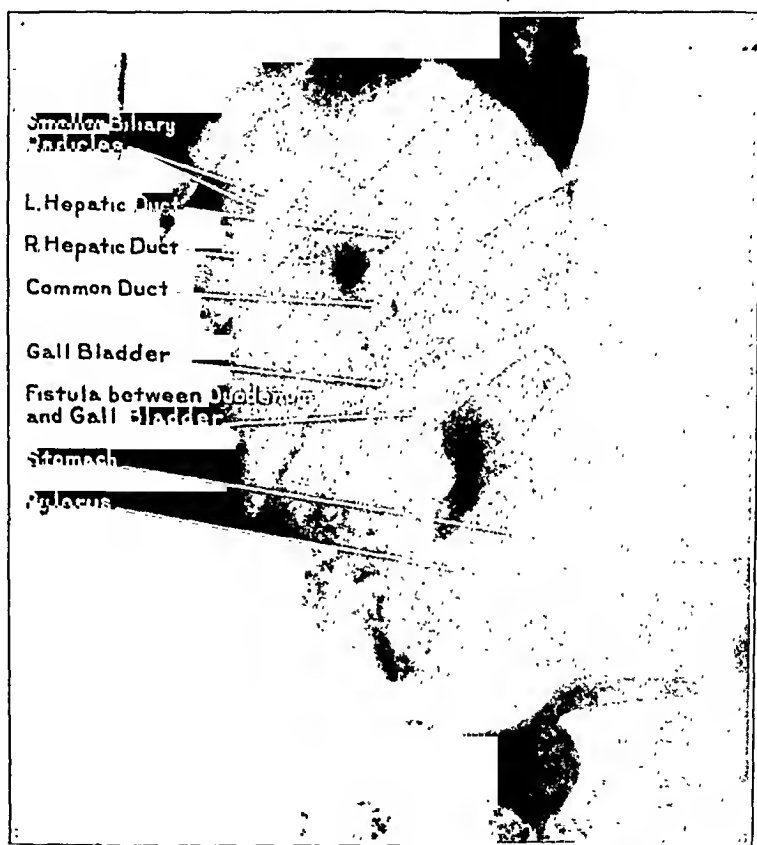


Fig. 2.—Following a meal of barium sulfate, a roentgenogram of the stomach, gallbladder and liver region revealed a barium fleck independent of the stream of barium sulfate about the second portion of the duodenum, which was interpreted as a fistulous opening between the gallbladder and duodenum, and air was seen in the extrahepatic biliary ducts and biliary radicles.

The patient was hospitalized and treated symptomatically, and an attempt was made to bring his diabetes under control. On about the sixth day, one of us (D. C. D.) was called into consultation. Flat roentgenograms of the abdomen were taken following instillation of dye into the gallbladder. A series of roentgenograms of the gastrointestinal tract and studies after a barium sulfate enema were made. A roentgenogram of the gallbladder failed to visualize a gallbladder

shadow, but there was a shadow representing a dilatation of the common and hepatic ducts. This shadow extended into the hepatic area as a branched shadow representing the larger and smaller bile radicles. The colon was dilated; otherwise it was normal. The fluoroscopic examination of the stomach and duodenum, including flat roentgenograms, showed that they were normal except that on fluoroscopic examination a barium speck, separated from the stream of barium sulfate, was seen in the upper wall of the second portion of the duodenum. It

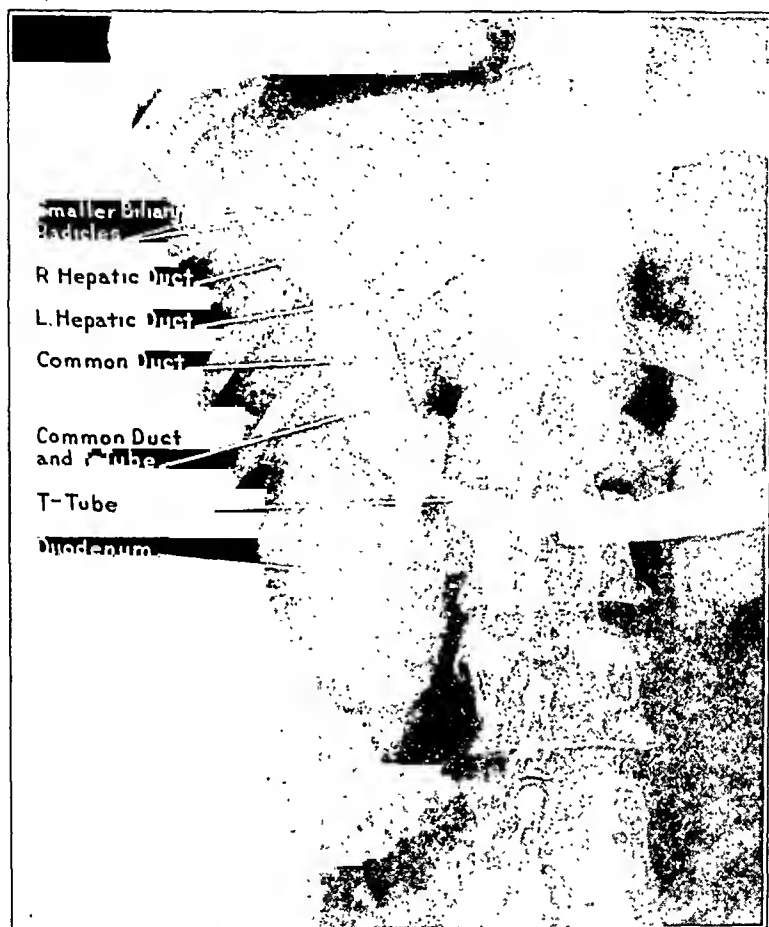


Fig. 3.—A roentgenogram made six weeks following operation. A 10 per cent solution of sodium iodide was injected into the T tube; the opaque material is seen to fill the common and hepatic ducts and liver radicles and to enter into the lumen of the bowel.

could not be dislodged from its bed by external manipulation of the abdomen. This was thought to be an opening of the fistula into the bowel.

#### OPERATION

With the patient under spinal anesthesia supplemented with cyclopropane, the abdomen was opened through an incision in the right upper rectus. The stomach and pylorus were free of pathologic changes. The greater portion of the duodenum was found firmly adherent to the right lobe of the liver. Due to the density of



the adhesions, much effort and time were spent in releasing the bowel from the liver. The gallbladder was found to be small and fibrotic and free of stones and its fundus firmly adherent to the duodenum. On release of the gallbladder from the bowel, an opening, or communication, between the two organs was seen. The fistulous opening in either organ did not exceed 3 mm. in diameter. The opening in the bowel was closed by first enlarging the fistulous opening in the bowel to obtain good exposure. It was then closed in a transverse manner, O chromic enterostomy suture being used for the mucous coat. Similar suture for the mus-

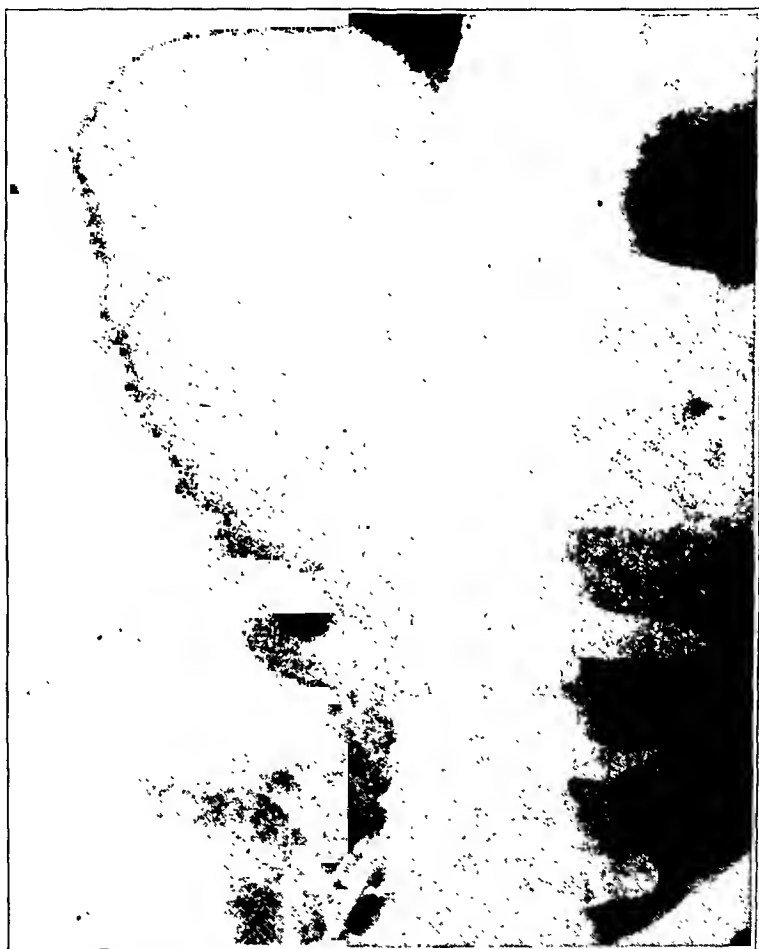


Fig. 4.—Flat roentgenogram of the upper part of the abdomen made approximately eight months following operation, after the patient was well and had returned to work, shows a normal outline of the liver and no dilatation of the extrahepatic ducts or biliary radicles.

cular and serous coats and the suture line was reenforced with interrupted cotton suture. The gallbladder contained much necrotic material. The cystic duct was patent, and the common duct was dilated to several times its normal size. Its walls were thickened and tense from intraluminal pressure, and, on aspiration of the common duct, approximately 10 to 15 cc. of air or gas was withdrawn before the light-colored bile fluid, mixed with flakes of debris, appeared in the

syringe. The common duct was opened for a distance of 3 to 4 cm. under guidance of stay sutures of cotton placed in either side of the wall of the duct, at such points to permit good exposure when opened. On incision of the duct, an additional amount of gas and air, with debris, escaped. Further exploration of the duct revealed a large amount of sandstone in its lower end. This was removed with a scoop and followed by irrigation of the duct with isotonic solution of sodium chloride. The upper end of the common and hepatic ducts was free of stone pigment. The patency of the common duct was established by passing a medium-sized probe through the ampulla and sphincter of Oddi into the bowel. A T tube was placed in the common duct, and its long flange end was permitted to escape through the sphincter of Oddi into the lumen of the bowel. The opening of the common duct was then closed with interrupted chromic surgical gut suture to the level where the tube made its escape, and the gallbladder and cystic duct were removed. All raw surfaces opposite the common duct and bed of the gallbladder were closed with running OO plain surgical gut suture. A Penrose drain was placed in the gallbladder fossae, and this was allowed to emerge from the abdomen through a counteropening in the lateral wall of the abdomen. The T tube was brought through the upper angle of the incision, with closure of the wound by the layer method.

The patient's surgical convalescence was an uninterrupted one. His low nutritional status was cared for by multiple blood transfusions and parenteral administration of amino acids. The Penrose drain was removed by the eighth day, having been shortened on alternate occasions. The T tube was worn for three months following the operation.

Culture of the aspirated bile from the common duct revealed growth of *Bacillus coli* and *Bacillus proteus* after twenty-four hours' incubation.

#### CONCLUSION

1. The physiologic and pathologic features of spontaneous internal biliary fistula have been discussed.

2. Review of the literature shows that due consideration has not been given the clinical picture and the importance of evaluation of the different biliary antecedents as a diagnostic aid in internal biliary fistula, but, instead, more attention has been directed to the roentgenologic findings for diagnosis.

3. Because of early fibrosis and contraction of the fistula, only in a small per cent of internal biliary fistulas will roentgenograms alone show the fistula.

4. To increase the percentage of diagnosis commensurable with the number of fistulas found at the operating table, we suggest that in addition to roentgen studies more attention be given to the clinical picture.

5. Early diagnosis based on the presumptive signs and roentgenologic studies and maintenance of a good surgical program are the best means of combating the problems of internal biliary fistula.

6. The points of interest in the case reported are the preoperative findings, clinical picture and visualization of air in bile passages and cure of the fistula.

## ARREST OF GROWTH OF THE EPIPHYSES

JOHN T. HODGEN, M.D.

AND

CHARLES H. FRANTZ, M.D.

GRAND RAPIDS, MICH.

**A**RREST of epiphysiodiaphysial growth, or epiphyseodesis, originally described by Phemister<sup>1</sup> in January 1933, having proposed as a method of obtaining equalization of leg length in growing children. This procedure involves the removal of a block of bone in length and 1.5 cm. in width from across the epiphysial line. The block is about 0.5 cm. deep. After removal of the block of bone the epiphysial line is curetted for a distance of 2 to 5 cm. lateralward for about 10 to 15 mm. in depth. It is the experience of Hatcher that stripping of the periphery of the epiphysial line is sufficient and deep curettement is unnecessary. The block of bone is then turned end on end and reinserted, so that a bony bridge covers the epiphysial line (fig. 1 B).

There have naturally arisen modifications of the original technique. Philip Wilson<sup>2</sup> went a step farther in cauterizing the epiphysial line after curettement. J. Warren White<sup>3</sup> devised a hollow, square chisel  $\frac{1}{2}$  inch (1.2 cm.) on a side, which he taped through the epiphysial line diagonally, so that two corners cut through the line and two corners cut on either side of the line (one distally and one proximally). The chisel cuts  $\frac{3}{4}$  inch (2 cm.) deep. After removal of the block of bone the adjacent portions of the epiphysial line are thoroughly curetted. The chisel is then rotated 90 degrees and reinserted and the block of bone is placed into place by means of a loosely fitting obturator in the shaft of the instrument. This results in a bony bridge across the epiphysial line (fig. 1 A). Haas<sup>4</sup> reported the use of rustless steel wire looped

From the Orthopedic Service of Blodgett Memorial Hospital.

1. Phemister, D. B.: Operative Treatment of Longitudinal Growth of the Bone in the Treatment of Deformities, *J. Bone & Joint Surg.* **15**:1 (Jan.) 1933.

2. Wilson, P. D., and Thompson, T. C.: A Clinical Consideration of Methods of Equalizing Leg Length, *Ann. Surg.* **110**:992 (Dec.) 1939.

3. White, J. W., and Stubbins, S. G., Jr.: Growth Arrests for Equalizing Leg Lengths, *J. A. M. A.* **126**:1146 (Dec. 30) 1944. White, J. W.: A Practical Graphic Method of Recording Leg Length Discrepancy, *South. Med. J.* **33**:381 (Sept.) 1940. White, J. W., and Warner, W. P., Jr.: Experiences with Epiphyseal Growth Arrests, *ibid.* **31**:411 (April) 1933.

4. Haas, S. L.: Retardation of Bone Growth by a Wire Loop, *J. Bone & Joint Surg.* **28**:25 (Jan.) 1945.

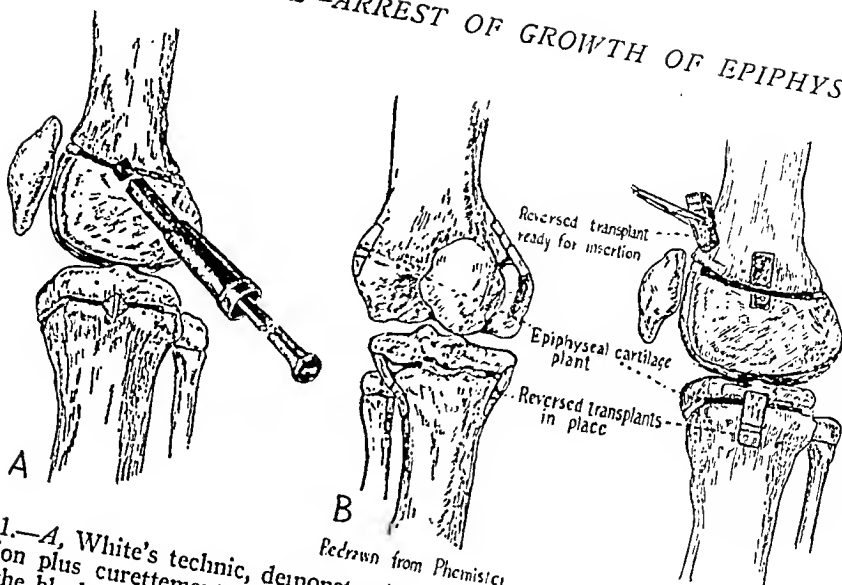


Fig. 1.—A, White's technic, demonstrating the rectangular block and 90 degrees of rotation plus curettement. Note the hollow obturator employed, the operator tapping the block of bone into its bed. B, Phemister's technic of curettement and reversal block method (Campbell, W.: Operative Orthopedics, St. Louis, C. V. Mosby Company, 1939).

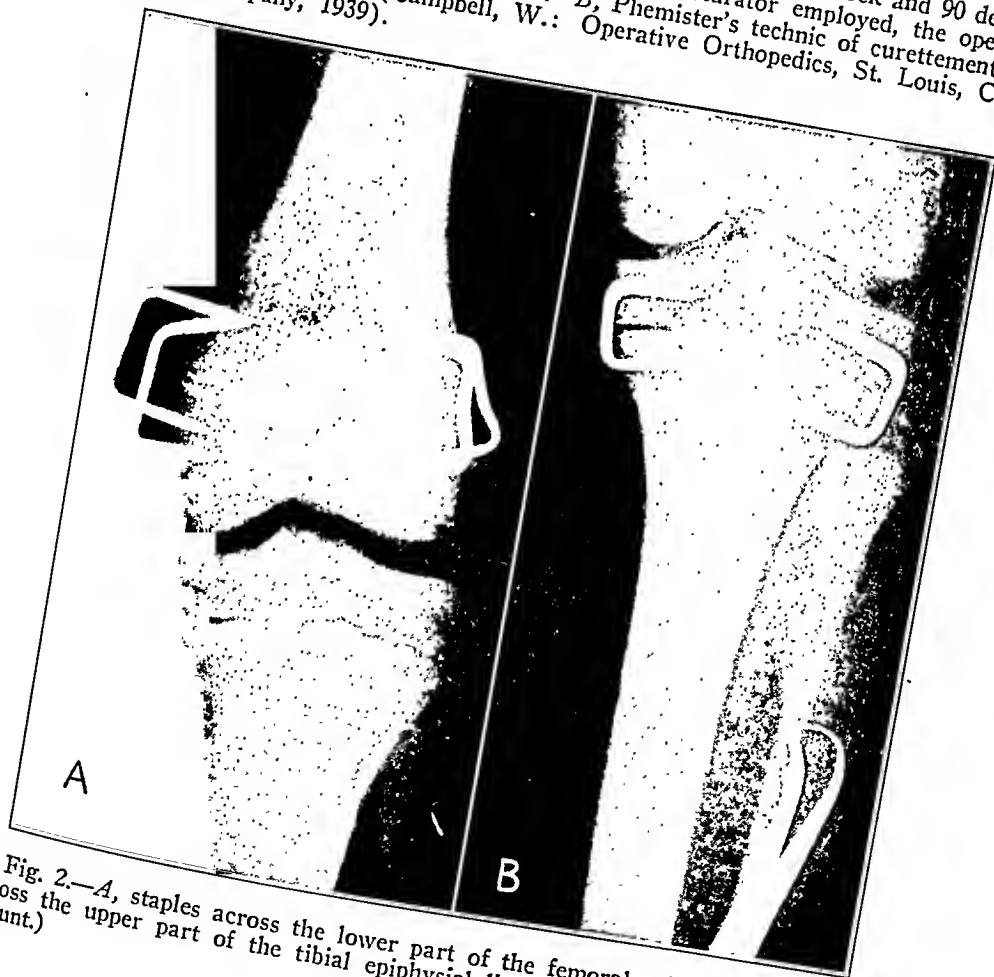


Fig. 2.—A, staples across the lower part of the femoral epiphysis. B, staples across the upper part of the tibial epiphysal line. (Courtesy of Dr. Walter P. Blount.)

the distal femoral epiphysis to slow growth. He successfully retarded growth in length without destroying the epiphysis. The wire may be removed when the desired result has been obtained. Blount<sup>5</sup> recently developed a technic utilizing the rational of Haas's wire loop. He simplified the true retardation process, without epiphysial destruction, by employing staples of stainless steel similar to those of R. E. Burns

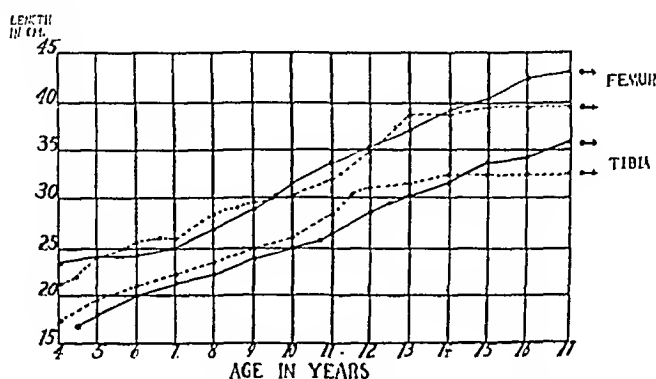


Fig. 3.—Growth increment curve of Hatcher.

(fig. 2). To date, all indications seem to prove that the method is efficient in arresting growth.

#### CALCULATION

The most difficult and yet the most important phase of this operation is determining the time for operation and in which epiphysis or epiphyses growth is to be arrested.

TABLE 1.—Average Normal Figures for Growth Expectancy of the Lower Extremities

| Age     | Male \ |       | Female |      |
|---------|--------|-------|--------|------|
|         | Cm.    | Inch  | Cm.    | Inch |
| 7.....  | 28.68  | 11.55 | 21.05  | 8.42 |
| 8.....  | 26.47  | 10.55 | 18.39  | 7.35 |
| 9.....  | 23.26  | 9.3   | 16.02  | 6.4  |
| 10..... | 20.14  | 8.06  | 12.16  | 4.86 |
| 11..... | 17.07  | 6.82  | 8.37   | 3.34 |
| 12..... | 14.34  | 5.73  | 6.40   | 2.66 |
| 13..... | 10.70  | 4.28  | 3.51   | 1.6  |
| 14..... | 7.27   | 2.9   | 1.80   | 0.72 |
| 15..... | 4.24   | 1.7   | 0.52   | 0.2— |
| 16..... | 2.09   | 0.83  | 0.14   |      |

A complete knowledge of skeletal growth and maturity in children has not as yet been reached, and there are factors over which the surgeon has no control. However, over a period of years, growth expectancy tables (table 1), developmental curve graphs (fig. 3) and clinical records have given the clinician guides with which to work.

5. Blount, W. P.: Personal communication to the authors.

Still, probably many surgeons are reluctant to embark on this operation because of the mathematical variations and, in some minds, uncertainty of results. It is realized that these growth expectancy curves and length of bones of lower extremities, as recorded by Baldwin<sup>6</sup> and Hatcher, Meredith and Gill and Abbott,<sup>7</sup> are averages, but they are working scales and the results obtained by consulting them in calculations are good. The surgeon naturally wishes a perfect result, but he is not seeking mathematical accuracy in equalizing limbs. Rather, he seeks a noticeable improvement in limb length that need not be 100 per cent perfect in measurement to be labeled a good clinical result.

A constant factor in the growth of the lower extremity is the contribution of each of the epiphyses: upper femoral, 12 per cent; lower femoral, 40 per cent; upper tibial, 27 per cent, and lower tibial 21 per cent. These figures may vary in chondrodysplasia.

It has been determined that girls do not grow after menstruation has begun and that they mature earlier than boys. Generally speaking, arrest of growth of the lower femoral epiphysis will retard growth of the limb  $\frac{3}{8}$  inch (0.9 cm.) per year, and arrest of growth of the proximal tibial epiphysis retards growth of the limb  $\frac{1}{4}$  inch (0.6 cm.) per year. Wilson<sup>8</sup> considers boys to stop growth at 16 years and girls at 14 years, and one finds in checking growth increment curves (fig. 3) that the increase in length of long bones tapers off to the horizontal at these ages.

In view of the variable factors involved in predictions of growth and in an endeavor to minimize these inaccuracies, every child who is a candidate for arrest of epiphysal growth should have an evaluation of skeletal maturation. This is accomplished by a roentgenogram of the carpal development, as scaled by Todd.<sup>9</sup> If the chronologic age varies six months or more, the bone maturation age is used in the calculations. We have seen variations in bone age and chronologic age of one year in youngsters of approximately normal weight, height and sexual development for their chronologic age.

6. Baldwin, B. T.: *Physical Growth of Children from Birth to Maturity*, in *Studies in Child Welfare*, Iowa City, University of Iowa, 1921, vol. 1, no. 1.

7. Gill, G. G.: *The Cause of Discrepancy in Length of the Limbs Following Tuberculosis of the Hip in Children: Arrest of Growth from Premature Closure of the Epiphyseal Cartilages About the Knee*, *J. Bone & Joint Surg.* **26**:272 (April) 1944; *A Simple Roentgenographic Method for the Measurement of Bone Length: A Modification of Milliwhee's Method of Slit Scanography*, *ibid.* **27**:767 (Oct.) 1944. Gill, G. G., and Abbott, L. C.: *Practical Method of Predicting Growth of the Femur and Tibia in the Child*, *Arch. Surg.* **45**:286 (Aug.) 1942.

8. Straub, L. R.; Thompson, T. C., and Wilson, P. D.: *The Result of Epiphyseodesis and Femoral Shortening in Relation to Equalization of Limb Length*, *J. Bone & Joint Surg.* **27**:254 (April) 1945.

9. Todd, T. N.: *Atlas of Skeletal Maturation (Hand)*, St. Louis, C. V. Mosby Company, 1937.

## MEASUREMENT

The universal method of measuring leg length is probably straight line mensuration by metal tape from the anterior-superior spine of the ilium to the medial malleolus at the ankle. This procedure is often checked when discrepancy in leg length exists by block lifts placed under the short limb, leveling the pelvis to the horizontal plane. These two methods are purely clinical and are subject to the error of personal equations. Two examiners will often vary slightly in their measurements, both of limb length and of discrepancy of length.

Roentgenologic examination has been used to measure more accurately lengths of the long bones. By employment of a series of teleroentgenograms, actual progress in growth is recorded and preserved. Phemister's<sup>1</sup> original article included measurements of the diaphyses of the bones involved by teleroentgenographic examination of the entire lower extremity.

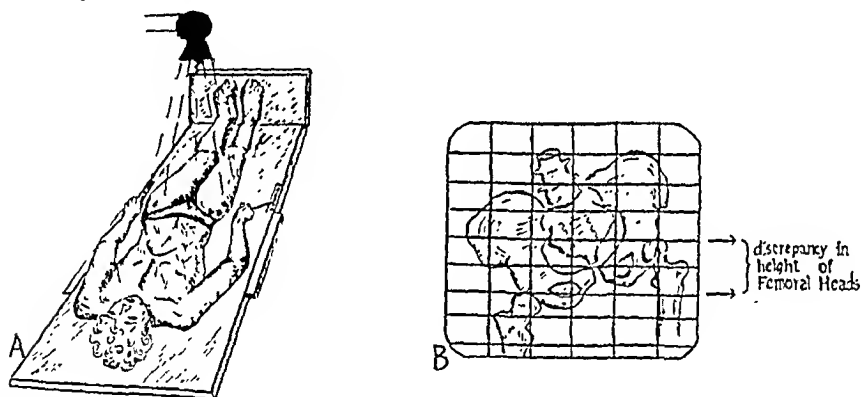


Fig. 4.—*A*, recording discrepancy in leg length by pelvic tilt and height of the femoral heads (after J. W. White). *B*, drawing of roentgenogram, with shadow of wires in cassette.

It is possible, therefore, to utilize roentgenologic examination in recording limb length and discrepancy as a check on purely clinical mensuration. Two practical methods have been developed. J. Warren White<sup>3</sup> records discrepancy only, by taking a flat roentgenogram of the pelvis. The patient is placed on the x-ray table and, by means of straps attached to the sides, pulls himself firmly against the foot plate, so that the two feet exert equal pressure (fig. 4). A flat roentgenogram is taken, a Bucky diaphragm being employed with the tube at the usual distance. The exertion of pressure by the short leg will cause a compensatory tilt in the pelvis and will be recorded on the plate. Originally, White determined the discrepancy by drawing tangents to the femoral heads and measuring with a celluloid triangle. This has been modified by placing horizontal and vertical wires in the cassette. Distortion will be present, as the cassette is some 2 inches (5 cm.)

below the table top and the femoral heads are 3 inches (7.6 cm.) above. This is a 5 inch (12.7 cm.) total. Ordinarily, the tube-cassette distance is 30 inches (76.2 cm.), giving 20 per cent magnification. The markers in the cassette tend to cancel out discrepancies, as the markers remain constant. A simple modification of this procedure can be pursued under fluoroscopic examination. With the patient exerting pressure on both feet, blocks of known thickness are placed under the foot of the short side, leveling the pelvis. This leveling is checked by horizontal wires in the fluoroscopic field. No correction need be made; the total block thickness is recorded on the patient's chart.

Gill<sup>7</sup> has modified Milliwee's method of slit scanography to obtain actual roentgenologic records of the length of the long bone. The tube moves from the hip distalward at the rate of 36 inches (91 cm.) per ten seconds by means of a rope and pulley attached to a weight. The quality of the roentgenogram is best with the tube distance at 30 inches. Error of distortion is not more than 2 per cent.

It is of importance to call attention to the fact that children under 8 years of age with excessive shortening due to tuberculosis of the hip or old septic arthritis need careful study. Gill has shown that premature closure of the epiphyses about the knee occurs in such cases. A child falling in this category should have the epiphyses about the knee of the involved side studied by roentgenographic examination. Characteristic contours reveal premature fusion. We believe that one of our earlier patients operated on fell into this group. Little change in discrepancy results after five years. We feel now that the epiphyses about the knee of the short leg, from which we expected future growth, had prematurely fused prior to the time of the arrest of the epiphysal growth on the normal side.

The method usually employed to determine which epiphysis to obliterate is based on the percentage of length now lacking on the short side in relation to the total expected growth of the limb. A simple formula is:  $\frac{\text{Shortening present}}{\text{Expected growth}} = \% \text{ of growth to eliminate.}$

A clinical example follows: A boy 10 years of age has 2 inches of shortening in the left leg. The problems of calculation are three: What is his expected growth? What per cent of growth is to be eliminated on the normal side? What epiphysis is to be obliterated? Consulting the table of growth expectancy, one finds that a boy of 10 years expects 20.14 cm. (8.06 inches) of growth before his maturity is reached. The formula now resolves itself into figures:  $\frac{2.00}{8.06} = 25$  per cent. It is revealed that to expect equalization of the legs at maturity 25 per cent of the growth of the normal side should be obliterated. The upper tibial epiphysis contributes 27 per cent to the growth of the leg. This is the closest value to the calculated figure. In these circumstances, arrest of the proximal tibial epiphysis will gain



the desired result. By postponing the operation until the patient has reached  $10\frac{1}{2}$  years, one finds the expectancy to be 18.61 cm. (7.40 inches). Thus,  $\frac{2.00}{7.40} = 27.1$  per cent of growth to be obliterated—a closer estimation—and is satisfactorily accomplished by operation on the proximal tibial epiphysis.

During the earlier years of this operation, errors on the conservative side have been prevalent; the surgical operation having been performed too late resulted in a permanent discrepancy after maturity. The ages of 10 to 12 years seem to be optimum for epiphysial fusion in cases in which 2 inches of shortening exists; double fusion at 12 years (distal femoral and proximal tibial) will bring approximal equalization of legs at 16 years of age.

#### TECHNIC

Surgical technic must be painstaking and solid union of turned blocks insured. A dry field for clear visualization of the epiphysial line is essential and is obtained by employing a pneumatic tourniquet at 6 to 8 pounds' (2.7 to 3.6 Kg.) pressure. An Esmarch bandage was used only on the first few patients. Elevation of the extremity to an almost vertical position during preparation of the skin suffices. The tourniquet is pumped to required pressure immediately after preparation of the skin, and the limb is lowered to the operating table for draping. Beginning laterally, one notices that the fascia lata is taut in extension; slight flexion of the knee will release tension and facilitate retraction for better visualization of the distal femoral epiphysial line. Care must be exercised in cutting the block outline through cortical bone. A sharp osteotome of  $\frac{1}{2}$  inch (1.2 cm.) is used, being angled into the cortex to prevent splintering, especially in the transverse cuts. It is important that the rotated end and refitted cortical block fit snugly to insure fusion. It can be gently impacted by blows with a small-headed mallet. After curettement and reinsertion of the block of bone in the lateral aspect, the medial aspect is exposed and the technic repeated. Obviously, a team of two operators reduces the time element in operating on medial and lateral aspects simultaneously. The approach to the upper fibular epiphysis and lateral aspect of the upper tibial epiphysis is slightly more difficult technically. Caution in exposure is necessary to prevent injury to the peroneal nerve. At least a 4 inch (10 cm.) incision is necessary. If the dissection is carried along the medial anterior border of the biceps femoris tendon, the periosteum being retracted outward and away from the fibular head, the peroneal nerve follows in the soft tissues and is lateral to the fibular head and field of operation. The fibular epiphysis can be excised. The wound is closed in layers and a pressure bandage applied over sterile dressings. Sterile sheets of cotton batting bound snugly with elastic bandage

suffice. Warren White immobilizes the limb in a plaster from groin to ankle for a period of three weeks. Others, however, employ no plaster dressing, allowing patients up in seven to ten days. Our practice has been to allow patients to dangle their legs over the bed when stitches are removed and to use crutches in ten days.

Blount's staples are made from  $\frac{3}{32}$  inch (0.2 cm.) rods of chrome nickel stainless steel. The limbs are  $\frac{3}{4}$  inch (1.9 cm.) and the cross member  $\frac{1}{2}$  inch (1.2 cm.). Exposure of the epiphysis is essentially the



Fig. 5.—The clinical deformity.

same as described in the aforementioned technic. Two staples are introduced on a side,  $\frac{1}{2}$  inch apart. It is unwise to allow the metal to straddle any structures of soft tissue other than periosteum. Blount stated that it is better to bury the staple under periosteum, thereby assuring firm fixation and lessening the possibility of loosening and gradual working out. Roentgenologic control is utilized throughout the operation. After closure of the incisions, a long plaster of paris cast is applied to the leg, including the foot, and remains on for three weeks. Walking is permitted as soon as the patient wishes.

The closure of the epiphysis is checked by roentgenograms three to six months postoperatively. This will warn of nonclosure and develop-

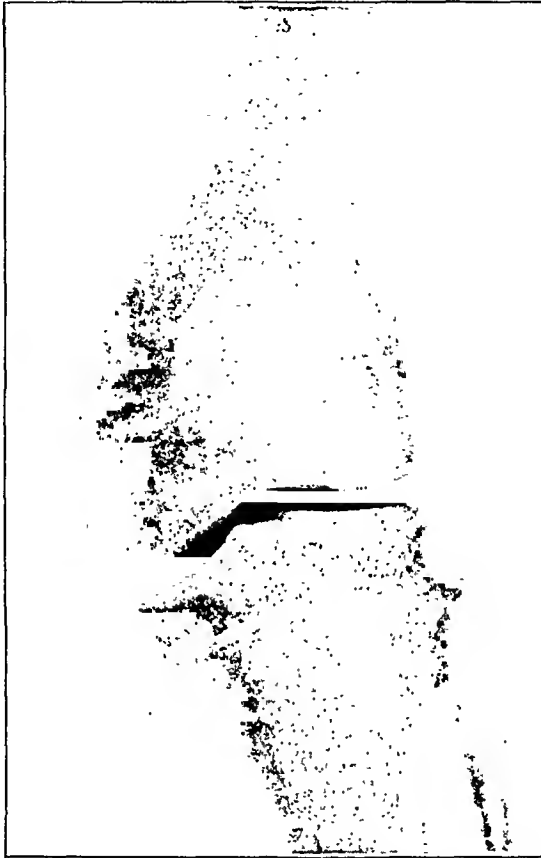


Fig. 6.—A roentgenogram of the patient in figure 5 revealed asymmetric fusion of the lower femoral epiphysis and relative overgrowth of the medial femoral condyle.

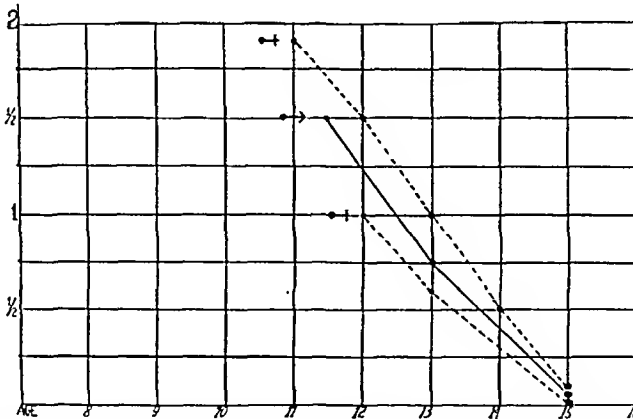


Fig. 7.—Arrest of growth of the distal femoral epiphysis for shortening in residual anterior poliomyelitis. Age at operation and discrepancy, with gradual equalization over a four year period.

ment of deformity, which may be prevented by a second operation. As a rule, deformity will appear in eighteen months. Asymmetric fusion results in deformity about the knee. Cases of genu recurvatum, varus and valgus have occurred. In 1 of the patients in this group a knock knee developed (later corrected by osteotomy) (figs. 5 and 6). To date we have not seen the side operated on shorter at maturity than the originally involved extremity.

## RESULTS

Results naturally cannot be evaluated until the subjects reach or closely approximate skeletal maturity. Clinical measurement of the legs is a satisfactory method for all practical purposes. Lift blocks

TABLE 2.—*Analysis of Twenty-One Cases in Which Operation Was Done by Phemister's Method*

| Case      | Age, Yr. | Sex | Short, In. | Final Short, In. | Operation  | Correc-<br>tion,<br>% |
|-----------|----------|-----|------------|------------------|--|-----------------------|
| E. B..... | 13       | F   | 2.0        | 1.5              | Lower femoral epiphysis  | 25                    |
| E. R..... | 10       | M   | 1.75       | 1.0              | Upper tibial epiphysis   | 40                    |
| L. D..... | 9.6      | M   | 2.25       | 0.5              | Upper tibial epiphysis   | 80                    |
| I. S..... | 12       | F   | 1.0        | 0.0              | Lower femoral epiphysis  | 100                   |
| E. B..... | 13       | F   | 2.0        | 0.75             | Lower femoral epiphysis and<br>upper tibial epiphysis              | 64                    |
| D. P..... | 14       | M   | 2.25       | 1.00             | Lower femoral epiphysis and<br>upper tibial epiphysis              | 60                    |
| O. R..... | 12       | M   | 2.50       | 0.0              | Lower femoral epiphysis  | 100                   |
| B. L..... | 8.5      | F   | 1.75       | 0.5              | Upper tibial epiphysis   | 80                    |
| B. L..... | 11       | F   | 1.75       | 0.0              | Upper tibial epiphysis   | 100                   |
| L. T..... | 11.5     | M   | 1.75       | 0.0              | Upper tibial epiphysis   | 100                   |
| H. H..... | 11.5     | M   | 1.50       | 0.0              | Lower femoral epiphysis  | 100                   |
| A. S..... | 13       | F   | 1.25       | 0.75             | Lower femoral epiphysis  | 40                    |
| J. V..... | 11.5     | F   | 2.0        | 1.0              | Upper tibial epiphysis   | 50                    |
| G. K..... | 12.5     | M   | 1.25       | 0.25             | Upper tibial epiphysis   | 80                    |
| J. S..... | 11       | F   | 1.50       | 1.0              | Lower femoral epiphysis  | 33                    |
| D. K..... | 9        | M   | 4.00       | 1.75             | Lower femoral epiphysis  | 57                    |
| R. D..... | 10.5     | M   | 2.50       | 0.75             | Upper tibial epiphysis   | 66                    |
| E. C..... | 13       | M   | 3.0        | 1.0              | Upper and lower tibial<br>epiphysis and lower<br>femoral epiphysis | 66                    |
| W. G..... | 12       | M   | 1.50       | 0.5              | Lower tibial epiphysis   | 80                    |
| B. W..... | 13       | F   | 1.0        | 0.0              | Lower femoral epiphysis  | 100                   |
| F. R..... | 11       | M   | 2.75       | 2.0              | Upper tibial epiphysis   | 29                    |

under the short side, leveling the pelvis, also afford a good clinical check. White's method or fluoroscopic check is more accurate and affords a permanent record of progress toward equalization of the limbs.

What is a "good" result? Clinical evaluation varies in different cases (fig. 7). A child with a 4 inch (10 cm.) discrepancy ending his extremity growth with  $\frac{3}{4}$  to 1 inch (1.9 to 2.5 cm.) shortening may be considered a good result. However, a 2 inch (5 cm.) discrepancy ending with 1 inch (2.5 cm.) shortening would seem only fair. Percentage of gain on the discrepancy may arbitrarily divide the results. A 75 per cent or more gain is a good result, 25 up to 75 per cent mediocre and less than 25 per cent poor.

Analysis of cases of 21 patients operated on after the method of Phemister, now at or near skeletal maturity, reveals the following figures:

|                                    | Patients, % |
|------------------------------------|-------------|
| Good result (75 to 100% gain)..... | 48          |
| Fair result (25 to 75% gain).....  | 47          |
| Poor result (0 to 25 % gain).....  | 5           |

The shortening was due to residual anterior poliomyelitis in 15 cases, old septic arthritis of the hip in 2 cases, old tuberculosis of the hip in 1 case and congenital or idiopathic shortening in 3 cases. It is to be noted that in 2 instances a double arrest was performed and in 1 instance a triple arrest.

#### COMMENT

End results will improve with increase in experience. Reluctance to operate at an early age should give way to energetic handling of the problem (average age at operation in this series is 11 years and 4 months). If anything, we have erred on the conservative side. The employment of evaluations of bone age and roentgenologic examination in recording discrepancy in leg length will aid in eliminating inaccuracies.

It is evident that arrest of epiphysial growth, despite the fact that it is an irreversible operation, should take its place with foot stabilization, tendon transference and bone grafting. The recent development of arresting staples by Blount has been a definite forward step in both preserving the life of the epiphysis and temporarily arresting growth. Further investigation of this technic after removal of the staples is aimed at answering two important questions: Will growth be resumed at the same rate as at the opposite epiphysis, and will growth continue as long as on the other side? The operation of arrest of growth of the epiphyses is another surgical aid to be employed in growing children for the correction of discrepancies in leg length due to congenital conditions, tumors, the results of trauma and the residuum of infectious diseases.

## SPONDYLOLISTHESIS

Additional Variations in Anomalies in the Pars Interarticularis

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**A**LONG with the accelerated tempo in investigations of syndromes of the lower part of the back during recent years, prespondylolisthesis and spondylolisthesis have been uncovered as relatively frequent findings. With reference to the defect in the neural arch, there has been speculation as to whether it has resulted from an intrauterine disturbance sufficient to fracture or to impede circulation to the isthmic portion, with the resultant defect of a pseudarthrosis, or whether there has been a developmental failure of bony fusion of the two separate ossification centers of this portion of the neural arch. We are prone to support the latter view and feel that other congenital anomalies of this isthmic portion may be present in addition. We seek to demonstrate some of these in the following presentation.

The defect in the neural arch referred to as spondylolysis or spondylolysis involves the isthmic portion, or pars interarticularis, situated between the superior and inferior articulating facets. In the "preslipping stage" and in the stage of actual forward dislocation of the vertebral body, the defect may involve only one side of the neural arch or both sides. When the defect involves only one side of the neural arch in a case of actual forward displacement of the vertebral body, a mechanical problem is posed. Moored as it is to the intact side of the neural arch, as demonstrated by posterior oblique roentgenograms, how can the vertebral body assume a position of forward dislocation, as demonstrated by lateral roentgenograms? If this were effected by rotation, both the lateral and the anteroposterior roentgenograms would demonstrate this. As will be seen later, they do not. The forward displacement in the face of one intact side must be explained on the basis of additional congenital anomalies.

In order clearly to demonstrate the variations in anomalies involving these particular lesions, the following types of cases will be presented: (1) defects in both sides of the neural arch without forward displacement of the vertebral body ("preslipping stage"); (2) defects in both

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sides of the neural arch with forward displacement of the vertebral body (spondylolisthesis); (3) defect in only one side of the neural arch without forward displacement of the the body ("preslipping stage"); (4) defect in only one side of the neural arch with forward displacement of the vertebral body (spondylolisthesis), and (5) reversed spondylolisthesis.

#### I. DEFECTS IN BOTH SIDES OF THE NEURAL ARCH WITHOUT FORWARD DISPLACEMENT OF THE VERTEBRAL BODY

Bilateral laminar defects without displacement constitute the entity described as the "preslipping stage," or prespondylolisthesis. The defects are easily demonstrated but the laminae are of sufficient integrity to maintain continuity of the neural arch and proper (normal) alignment of the related vertebral bodies. In this situation, clinical symptoms could be ascribed only to the fact that bony defects, although "intact," indicate the presence of associated defects of soft tissue and ligamentary defects and therefore a high degree of vulnerability of this particular part of the spine to strain forces. The imposition of severe enough trauma on this abnormal complex could disrupt its continuity completely, and the vertebra, freed from its moorings, would be displaced forward in proportion to the disruption force.

#### II. DEFECTS IN BOTH SIDES OF THE NEURAL ARCH WITH FORWARD DISPLACEMENT OF THE VERTEBRAL BODY

The complex seen in roentgenograms in a typical case is a forward displacement of the body in the lateral projection and a defect of the pars interarticularis on both sides in the right and left posterior oblique projections. The neural arch has been dissolved so far as normal mechanics are concerned, and the vertebral body, adrift, has moved under the descending weight of the spinal vertebrae, into a forward displacement. Findings on physical examination include the appearance of a shortening of the trunk, as though it had settled into the pelvis, prominence of the hips and a palpable, locally tender "step-off" in the alignment of the spinous processes as one's finger progresses over the sacrum upward along the midline of the back. These findings are in proportion to the extent of the anterior dislocation of the body. While the lateral roentgenographic projections later may disclose an increased lordosis of the lumbar portion of the spine, usually the lower part of the back on physical examination presents a rather flat appearance, understandable on the basis of the paravertebral muscles having become more superficially prominent as they are lifted up over the prominent sacrum. The masked lordosis is better appreciated on palpation in the midline upward from the "step-off." These conditions may or may not be clinically active. The causes of these phases of decompensation are varied: further displacement from trauma, general physical debility of a tem-

porary phase, transient myositis from strain and similar factors. This type most frequently requires spinal fusion. Case 1 illustrates a typical case.

CASE 1.—R. C. E. is a 25 year old white man giving a history of several injuries to the back prior to admission and presenting physical findings characteristic of the lesion. Conservative therapy has not allayed his symptoms, and he will undoubtedly require spinal fusion. In figure 1 *A* the anteroposterior projection discloses no visible defect in the neural arch. The lateral projection (fig. 1 *B*) shows the forward displacement of the fifth lumbar vertebra on the sacrum. The right posterior oblique projection (fig. 2 *A*) shows an absence of the right pars interarticularis, constituting a defect in the continuity of the neural arch. The



Fig. 1 (case 1).—*A*, anteroposterior projection. Slight condensation of bone is present about both lumbosacral joints. There is no visible defect in the neural arch. *B*, lateral projection. There is a 1 cm. anterior displacement of the body of the fifth lumbar vertebra, with moderate lipping of the anterior corner of the sacrum.

left posterior oblique projection (fig. 2 *B*) shows the left pars interarticularis to be present, but there is a defect near the base of the inferior articular facet. There is, in this instance, a bilateral spondyloschisis and spondylolisthesis, the former characterized by an absence of the pars interarticularis on one side and a failure of fusion with the lamina on the other side.

### III. DEFECT IN ONLY ONE SIDE OF THE NEURAL ARCH WITHOUT FORWARD DISPLACEMENT OF THE BODY

A unilateral laminar defect in the neural arch without displacement of the vertebral body is understandable. On one side, as viewed in the posterior oblique projection, there is a spondyloschisis. On the other, the pars interarticularis is of normal proportions and integrity. There could be no means of forward displacement unless in a limited way by rotation. The lateral projection in these cases shows a normal alinement of the involved body. Case 2 is an illustration of such a lesion.



CASE 2.—H. C. H. is a 40 year old white man who was admitted to the hospital with the complaint of pain in multiple joints, including the lower part of the back. On the basis of roentgenographic findings, he was sent to us as having a deformity of the lower part of the spine. Foci of infection were searched for, and after tonsillectomy he experienced definite improvement of all joints, including the lumbosacral region. The physical examination of his back on discharge was noncontributory. In figure 3 the anteroposterior projection (*A*) discloses an incomplete fusion of the lamina of the fifth lumbar vertebra at the base of the spinous process. The lateral projection (*B*) shows no anterior displacement of the body of the fifth lumbar vertebra. In the right posterior oblique projection



Fig. 2 (case 1).—*A*, right posterior oblique projection. There is absence of the right pars interarticularis, showing the unbroken line of the cephalad surface of the lamina extending backward from the inferior articular facet. There is downward displacement of the superior articulation of the fifth lumbar vertebra, so that it nearly impinges on the inferior articulation. *B*, left posterior oblique projection. The left pars interarticularis is present but shows a 2 mm. defect near the base of the inferior articular facet. Note that the line of the cephalad surface of the lamina is broken by the shadow of the pars interarticularis. In these and all subsequent illustrations, the arrow points to the region of the pars interarticularis of the fifth lumbar neural arch.

(*C*) the pars interarticularis appears well formed and solidly continuous throughout. The left posterior oblique projection (*D*) shows the left lamina to be less than one third the width of the right and to have no bony continuity with the superior articular facet. The left pars interarticularis is completely absent. This case, then, presents a unilateral defect not from failure of fusion of the pars interarticularis with the lamina but from a congenital absence of the former, unattended by any forward displacement of the vertebra—a unilateral spondylolysis without spondylolisthesis.

IV. DEFECT IN ONLY ONE SIDE OF THE NEURAL ARCH WITH FORWARD DISPLACEMENT OF THE VERTEBRAL BODY

In some instances there is a unilateral defect in continuity with forward displacement of the vertebral body. The oblique projections again show a spondyloschisis on one side and an intact pars interarticularis on

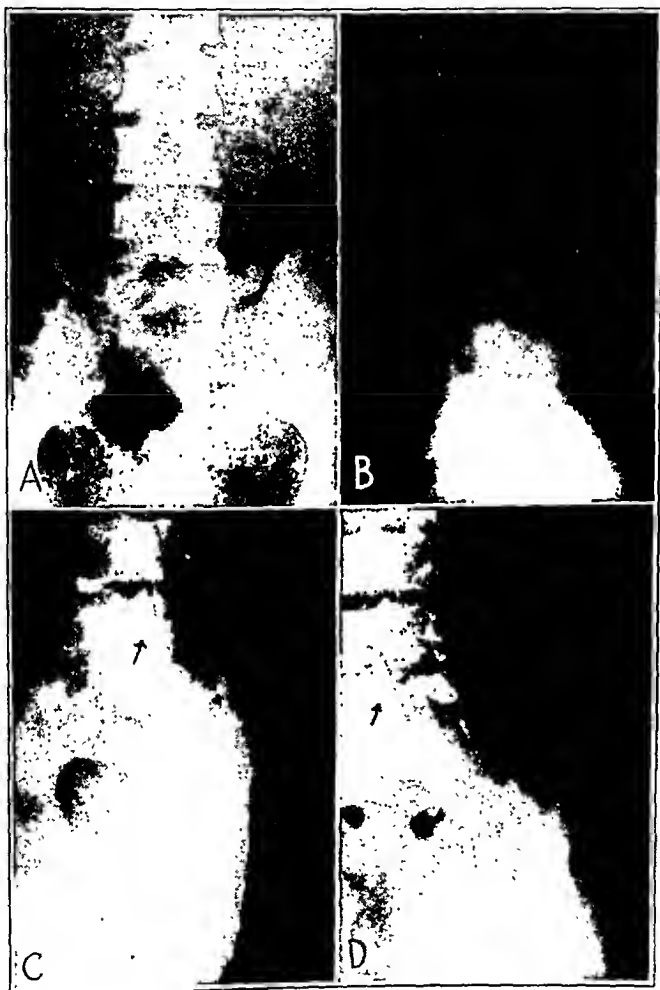


Fig. 3 (case 2).—*A*, anteroposterior projection. This view shows only an incomplete fusion of the laminae on the fifth lumbar space at the base of the spinous process. *B*, lateral projection. There is no anterior displacement of the body of the fifth lumbar space. *C*, right posterior oblique projection. This view shows the right half of the neural arch in profile. The pars interarticularis of the right lamina is shown to be well formed and solid throughout. *D*, left posterior oblique projection. This view shows the left lamina to be less than one third the width of the right one and to have no bony connection with the superior articular facet; in other words, the pars interarticularis is absent. The cephalad surface of the lamina forms a smooth, unbroken, horizontal line of cortical bone from the spinous process to the superior surface of the inferior articular facet, giving an appearance entirely different from the normal laminar outline on the right, where the cephalad surface of the lamina curves upward to the inferior surface of the superior articular facet.

the opposite side. There is no evidence of lateral bending or rotation, since the articular facets bear a normal relationship one to the other. What, then, is the mechanism allowing for the dislocation? Case 3 is an illustration of such a lesion.

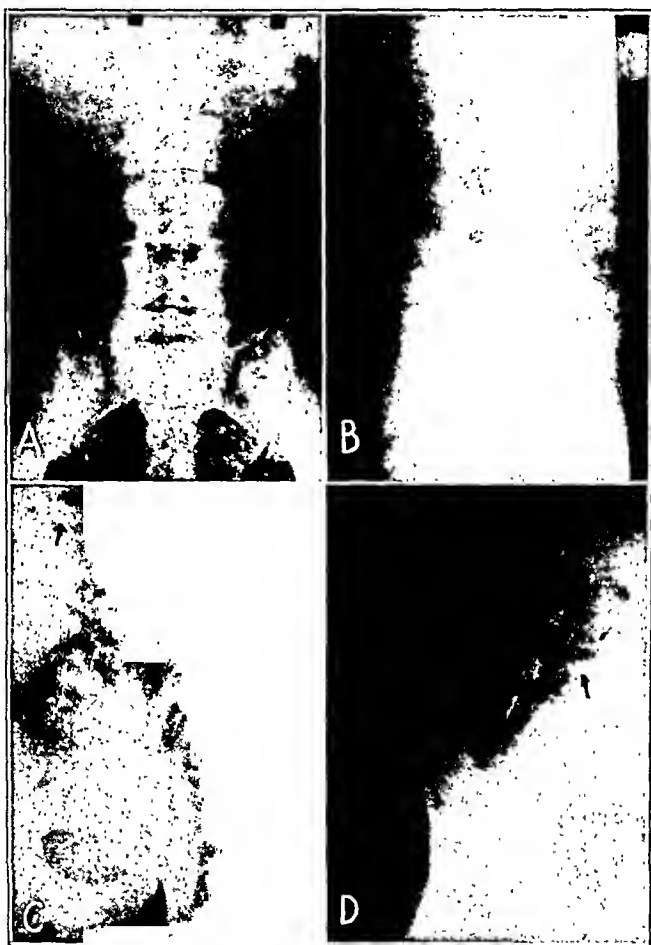


Fig. 4 (case 3).—*A*, anteroposterior projection. It is not remarkable. *B*, lateral projection. There is a 1 cm. anterior dislocation of the body of the fifth lumbar vertebra on the sacrum, with narrowing of the fifth lumbar disk by one half. Slight lipping of the anterior margin of the first sacral segment is present. *C*, right posterior oblique projection. The pars interarticularis of the right lamina is intact throughout (this is confirmed by stereoscopic views) but is unusually long and horizontal in position. *D*, left posterior oblique projection. The left pars interarticularis of the fifth lumbar space shows a definite defect of continuity near its midpoint, but the apparent separation of the parts is less than 2 mm. On this side also, the pars interarticularis is unusually long and horizontally placed.

CASE 3.—J. B. L. is a 34 year old white man who sustained an injury overseas when he fell from a dock, striking his left side against a crane. His immediate symptom was pain along the right costal margin, and, when, several days later, he complained of mild pain in the lower part of the back, roentgenograms were made and the spondylolisthesis was seen in the lateral view. He was admitted to the hospital on the basis of these roentgenologic findings and subsequently

returned to the mainland. On arrival, he stated that he was completely free from pain low in the back. Except for a prominence of the sacrum and an increased lordosis discernible on deep palpation along the spinous processes, physical examination was noncontributory.

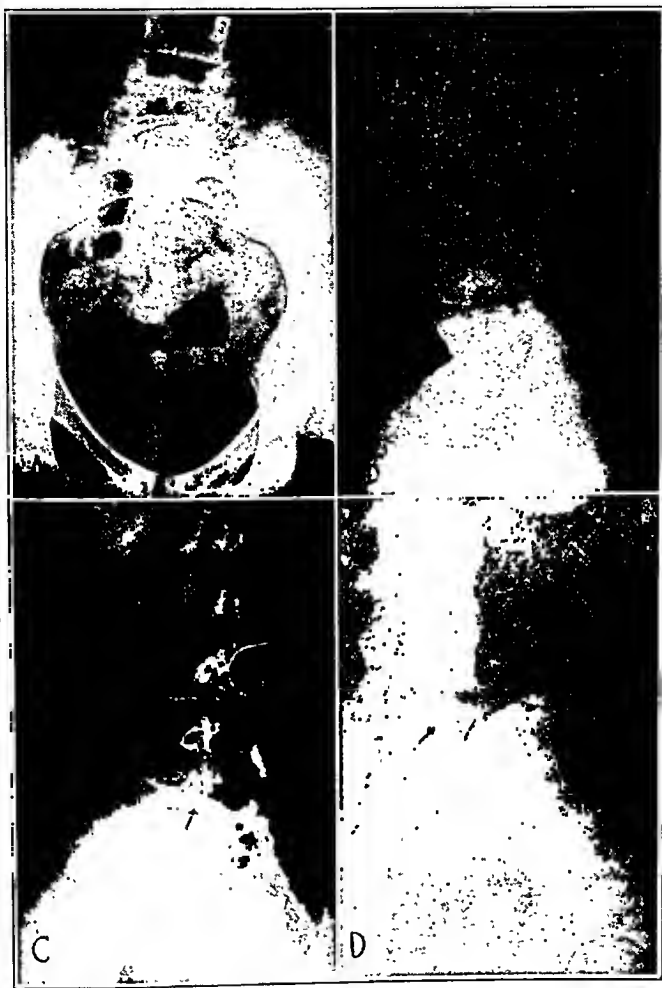


Fig. 5.—*A*, anteroposterior projection. It is normal except for incomplete formation of the spine of the fifth lumbar space. *B*, lateral projection. The body of the fifth vertebra is displaced posteriorly 2 mm. on the sacrum. *C* and *D*, right and left posterior oblique projections. Both interarticular portions of the neural arch of the fifth lumbar space are intact but are unusually short and almost vertical in position. On both sides the lumbosacral joint is anterior to the fourth lumbar intervertebral articulation instead of in the more usual posterior location. The displacement of the body of the fifth lumbar vertebra is therefore due to a bilateral congenitally short pars interarticularis of the neural arch and not to a schistasis of the arch.

In figure 4 the anteroposterior view (*A*) is not remarkable. The lateral projection (*B*) shows a 1 cm. anterior displacement of the fifth lumbar vertebra on the sacrum, with a narrowing of the fifth lumbar disk by approximately one half. In the right posterior oblique projection (*C*), the pars interarticularis of the right lamina is intact through-

out. This is confirmed by stereoscopic views. It is, however, unusually long (congenital elongation) and horizontal in position. The left posterior oblique projection (*D*) shows a 2 mm. defect in the pars interarticularis of the left lamina. This amount of separation is insufficient to account for the 1 cm. displacement of the body. While it is true that the real separation may be somewhat greater than the apparent separation, at least some of the displacement of the vertebral body is due to the unusual length and horizontal position of the pars interarticularis. Thus the anterior displacement of the vertebral body is due not so much to the unilateral bony defect as to the bilateral congenital elongation of the interarticular parts of the lamina.

#### V. REVERSED SPONDYLOLISTHESIS

In figure 5 the anteroposterior projection (*A*) is not remarkable save for an incomplete formation of the spinous process of the fifth lumbar vertebra. In the lateral projection (*B*), the body of the fifth lumbar vertebra is displaced posteriorly a measurable 2 mm. In the right and left posterior oblique projections (*C*) and (*D*), both interarticular portions of the neural arch of the fifth lumbar vertebra are intact, but both are unusually short and almost vertical in position. In this instance the posterior displacement or reversed spondylolisthesis of the body of the fifth lumbar vertebra is therefore due to a congenitally misshapen neural arch, with abnormal shortening of its interarticular parts.

#### CONCLUSIONS

Additional and correlated variations of the anomaly in the pars interarticularis or isthmic portion of the neural arch are demonstrated. These include congenital absence of the pars interarticularis, congenital lengthening of the pars interarticularis and congenital shortening of the pars interarticularis as well as the usual defect resulting from failure of fusion of the pars interarticularis with the lamina.

The mechanism for the dislocation of a vertebral body in the presence of a unilateral defect in continuity, involving one side only in the neural arch, is explained on the basis of a demonstrated congenitally elongated pars interarticularis on both sides.

A reversed spondylolisthesis in the presence of an intact neural arch and posterior articulations is demonstrated to be the result of a congenital shortening of the pars interarticularis bilaterally.

For a complete understanding of the exact nature of the anatomic variations, oblique as well as anteroposterior and lateral projections should be included in the roentgenographic study of disability low in the back. In cases of unilateral congenital spondyloschisis, without symptoms before injury to the lower part of the back, oblique views may reveal a recent fracture of the previously intact side. In cases of questionable symptoms, stereoscopic views are valuable.

## HIGH PROTEIN THERAPY

Clinical Effectiveness of Oral Administration of a New Protein Preparation  
As Determined by Nitrogen Balance Studies

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IN A RECENTLY reported study from this laboratory,<sup>1</sup> it was shown that positive nitrogen balances could be consistently obtained in surgical patients with protein deficiency by the parenteral administration of amino acids as the only source of nitrogen. However, this method was not successful as a practical program for restoration of the large losses of nitrogen incurred in the protracted deficiency of protein of such patients. With nitrogen losses estimated to be on the order of 480 Gm., the average positive nitrogen balance of 4 Gm. that was obtained would require one hundred and twenty days of continuous intravenous treatment for complete restitution of protein stores. Such management was obviously impractical if not impossible. The time required could be reduced, it was true, if parenteral injections were supplemented with blood transfusions and with normal oral alimentation.

The need for high intakes of protein or protein digests in patients with severe deficiency of nitrogen has been well recognized.<sup>2</sup> Successful efforts to meet this demand by intubation feeding of protein hydrolysates have been reported.<sup>2</sup> We, too, have frequently made use of

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From the Hektoen Institute for Medical Research of the Cook County Hospital and the departments of surgery of the Cook County Hospital, Northwestern University Medical School and the Cook County Graduate School of Medicine.

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2. Co Tui; Wright, A. M.; Mulholland, J. H.; Carabba, V.; Barcham, I., and Vinci, V. J.: Studies on Surgical Convalescence: I. Sources of Nitrogen Loss Postgastrectomy and Effect of High Amino Acids and High Caloric Intake on Convalescence, *Ann. Surg.* **120**:99, 1944.

3. Elman, R.: The Oral Use of the Amino Acids of Hydrolyzed Casein (Amigen) in Surgical Patients, *Am. J. Digest. Dis.* **10**:48, 1943. Lund, C. C., and Levenson, S. M.: Protein in Surgery, *J. A. M. A.* **128**:95 (May 12) 1945. Co Tui and others.<sup>2</sup>

such methods. However, feeding through an intranasal catheter is burdensome both to the patient and to the hospital staff. It is justified in the immediate postoperative period or other conditions in which normal feeding cannot be maintained, but its discomfort, the risk of esophagitis, the frequently accompanying diarrhea and the psychologic assault produced by the supplanting of normal eating habits with such an unnatural procedure make intubation feeding unsatisfactory. It has become increasingly clear that the ideal high protein therapy in patients able to take food by mouth is the oral administration of a palatable,

TABLE 1.—*Analysis of Essenaminc*

| Content             | Percentage |
|---------------------|------------|
| Total nitrogen..... | 12.5       |
| Moisture.....       | 6.5        |
| Fat.....            | 3.5        |
| Ash.....            | 1.9        |
| Chloride.....       | 0.03       |
| Calcium.....        | 0.06       |
| Phosphate.....      | 0.02       |
| Sulfate.....        | 0.2        |
| Iron.....           | 0.1        |
| Sodium.....         | 0.4        |
| Potassium.....      | 0.2        |

TABLE 2.—*Amino Acid Content of Essenaminc as Compared with That of Lactalbumin*

|                    | Essenaminc,<br>per Cent | Lactalbumin,<br>per Cent * |
|--------------------|-------------------------|----------------------------|
| Arginine.....      | 3.6                     | 3.5 ± 0.5                  |
| Histidine.....     | 2.2                     | 2.0 ± 0.3                  |
| Lysine.....        | 8.7                     | 8.0 ± 1.1                  |
| Tryptophan.....    | 2.5                     | 2.3 ± 0.3                  |
| Phenylalanine..... | 5.4                     | 5.6                        |
| Methionine.....    | 3.5                     | 2.8 ± 0.2                  |
| Threonine.....     | 6.8                     | 5.3                        |
| Leucine.....       | 12.0                    | 15                         |
| Isoleucine.....    | 7.5                     |                            |
| Valine.....        | 6.8                     |                            |
| Cystine.....       | 2.7                     | 3.0 ± 0.2                  |
| Tyrosine.....      | 4.6                     | 5.3 ± 0.1                  |

\* Block, R. J., and Bolling, D.: *The Amino Acid Composition of Proteins and Foods: Analytical Methods and Results*, Springfield, Ill., Charles O Thomas, Publisher, 1945, p. 303.

easily digested protein or protein derivative capable of being incorporated in large quantities in the common foods and of producing large positive nitrogen balances.

Recently a new processed protein, called Essenaminc, has been made available to us for study.<sup>4</sup> This product is a yellowish white, nonhygroscopic powder obtained by partial alkaline degradation of lactalbumin. It contains, by our analysis, 12.5 per cent nitrogen. Its content of amino acids, as furnished to us by the manufacturers and listed in table 1, indicates that it is a complete protein not significantly different in

4. Furnished by Frederick Stearns & Company, Detroit.

amino acid content from the lactalbumin from which it was prepared. It is only slightly soluble in water and is incorporated as a suspension in the solid or liquid food items of the diet. It has no odor and no pronounced taste. Its presence can easily be masked by other foods, except so far as it makes these foods "heavier" and dilutes their taste. The product appears to be stable indefinitely even when kept in bulk without any special precautions.

It was the purpose of this investigation to make a clinical evaluation of Essenaminate, first, by determining the minimal amount of Essenaminate required for nitrogen equilibrium and, second, by treating patients with large quantities of Essenaminate in addition to normal foods and ascertaining, through nitrogen balance studies and through determinations of plasma volume and serum protein levels, what degree of nitrogen retention and protein restitution was possible. At the same time an effort was to be made to determine whether the use of Essenaminate was a practical dietetic procedure.

#### METHODS

Fourteen surgical patients with protein deficiency who were able to take food by mouth were studied in a metabolic unit. This unit was staffed by special nurses over the twenty-four hour period and by special dietitians. Careful balance studies were carried out in which the foods were accurately weighed or measured and steps taken to see that the subjects cooperated by eating all the food offered them. All specimens of urine for the twenty-four hour periods were collected in bottles containing toluene. Stools were kept for analysis in large covered beakers containing toluene. When other excretions occurred, such as from fistulas, these were collected. The total excretions were analyzed for the twenty-four hour periods by micro-Kjeldahl methods as modified by Hoffman and Osgood.<sup>5</sup> The stools were first homogenized in water, with the aid of concentrated sulfuric acid, as suggested by Peters and Van Slyke.<sup>6</sup> The nitrogen content of the sample diets was similarly determined. Estimations of plasma volume were made by the Evans blue method, in which a single ten minute sample was used, as recommended by Gregerson.<sup>7</sup> The determination was carried out in the morning, breakfast having been withheld and no food given since the previous evening meal. Since none of the patients had any recognizable circulatory impairment, ten minutes was believed to be adequate for complete mixing of the injected Evans blue. Determinations of hematocrit levels were made on heparinized blood in Wintrobe tubes. Analyses of serum albumin were made by the method of Campbell and Hanna.<sup>8</sup>

Eleven of the 14 patients were first placed on the minimal Essenaminate diet. Later, when the minimal requirements for nitrogen balance had been determined,

5. Hoffman, W. S., and Osgood, B.: The Photoelectric Microdetermination of Nitrogenous Constituents of Blood and Urine by Direct Nesslerization, *J. Lab. & Clin. Med.* 25:856, 1940.

6. Peters, J. P., and Van Slyke, D. D.: Quantitative Clinical Chemistry, Baltimore, Williams and Wilkins Company, 1932, vol. 2, p. 78.

7. Gregerson, M. I.: A Practical Method for the Determination of Blood Volume with the Dye T-1824, *J. Lab. & Clin. Med.* 29:1266, 1944.

8. Campbell, W. R., and Hanna, M. I.: The Albumins, Globulins, and Fibrinogen of Serum and Plasma, *J. Biol. Chem.* 119:15, 1937.



9 of the same patients were placed on high Essenamined diets. In experiments with 3 additional patients, only the high Essenamined diet was used. In the latter group, the preparation of Essenamined used contained much more sodium chloride and less nitrogen than that used for all other experiments (see table 4), though it was prepared from lactalbumin in essentially the same manner.

The initial diet for the determination of the minimal protein requirement consisted of Essenamined mixed with foods which contained little or no nitrogen. It was found impossible to get the cooperation of the patients if the foods were such as to be completely devoid of nitrogen. Therefore a compromise had to be made by the use as vehicles for the Essenamined of the fruits and vegetables which contained 1 per cent or less of protein, as determined from accepted tables<sup>9</sup> and confirmed by nitrogen analyses. Though admittedly such a procedure could not have the same significance as that in which all other sources of nitrogen were rigidly excluded—as could be accomplished with laboratory animals or with normal human volunteers—it was unlikely that any great error was introduced, for the daily quantity of extraneous nitrogen represented only 6 to 7 per cent of the total nitrogen of the diet and the proteins involved were known to be of inferior biologic value. It was extremely unlikely that the small quantities of these proteins from leafy vegetables or from fruits could furnish significant amounts of any essential amino acids that might be missing from the Essenamined diet.

The food for the minimal diets was prepared in three forms: (1) a drink containing Essenamined, oil and sugar in an agar solution (when little water was used, the cooled preparation became a custard); (2) a sauce containing Essenamined, for vegetables or for use as a thick soup, and (3) a fruit "crisp" containing Essenamined. The method of preparation of these foods is given in the appendix. The diet furnished some 2,000 calories. Preliminary trials were made to determine the approximate quantity of Essenamined necessary for positive nitrogen balance, since it was impractical to place the patients on a graduated program, with increasing quantities of protein, such as was used by Allison<sup>10</sup> with dogs. The amount finally chosen was 60 Gm. of Essenamined, and this quantity was given regardless of the weight of the patients. An occasional failure of a subject to eat one of the food items sometimes modified this intake.

For the experiments with large amounts of Essenamined, the plan was to determine the extent of nitrogen retention and clinical improvement that occurred when Essenamined was given as a supplement to ordinary foods. The latter were kept as constant as possible and except for the milk used were relatively low in proteins. The nitrogen content of these foods was calculated from accepted tables<sup>9</sup> but was checked by sample analyses of the whole daily diet. The errors involved were too small to influence considerably the amount of positive nitrogen balance, particularly since the nitrogen of the milk of the diet, which constituted the chief portion of the extraneous nitrogen, was determined by direct analysis. Essenamined was given in most of the experiments chiefly in the form of a concentrated milk shake, which proved palatable. This drink was made to contain 150 Gm. of Essenamined per 1,500 cc., which was offered daily to the subjects. They were requested to drink a glass at a time during the day in addition to their small regular meals. Essenamined was also furnished in the form of cookies, biscuits or fruit pudding, all of

9. Chatfield, C., and Adams, G.: *The Proximate Composition of American Food Materials*, Circular no. 549, United States Department of Agriculture, 1940.

10. Allison, J. B., and Anderson, J. A.: *The Relation Between Absorbed Nitrogen, Nitrogen Balance and Biological Value of Proteins in Adult Dogs*, *J. Nutrition* 29:413, 1945.

TABLE 3.—*Minimal Essensamine Requirement for Nitrogen Balance*

| Case | Diagnosis                        | Weight,<br>Kg. | Days<br>on<br>Diet | Average Daily<br>Essensamine Intake |                 |            | Average<br>Additional<br>Nitrogen<br>Intake | Total<br>Nitrogen<br>Intake,<br>Gm. | Total<br>Nitrogen<br>Excretion,<br>Gm. | Nitrogen Balance |                        | Daily Intake per Kg.<br>Body Weight |                 |
|------|----------------------------------|----------------|--------------------|-------------------------------------|-----------------|------------|---|-------------------------------------|--|------------------|------------------------|-------------------------------------|-----------------|
|      |                                  |                |                    | Gm.<br>Protein                      | Gm.<br>Nitrogen | Gm.<br>Gm. |   |                                     |  | Total            | Gm. per Kg.<br>per Day | Gm.<br>Protein                      | Gm.<br>Nitrogen |
|      |                                  |                |                    |                                     |                 |            |   |                                     |  |                  |                        |                                     |                 |
| 1.   | Gastritis.....                   | 62.7           | 7                  | 72.8                                | 9.10            | 0.57       | 67.7  | 62.6                                | + 5.1                                  | 0.0126           | 1.16                   | 0.15                                |                 |
| 2.   | Carcinoma of the sigmoid.....    | 70             | 8                  | 75.0                                | 9.38            | 0.57       | 70.1  | 61.2                                | +17.9                                  | 0.0320           | 1.07                   | 0.14                                |                 |
| 3.   | Carcinoma of the stomach.....    | 49             | 9                  | 60                                  | 7.50            | 0.48       | 71.8  | 56.4                                | +15.4                                  | 0.0350           | 1.23                   | 0.16                                |                 |
| 4.   | Pelvic inflammatory disease..... | 49             | 9                  | 60                                  | 7.50            | 0.48       | 71.8  | 69.0                                | + 2.8                                  | 0.0132           | 1.23                   | 0.16                                |                 |
| 5.   | Carcinoma of the rectum.....     | 40             | 9                  | 48.7                                | 5.86            | 0.40       | 54.3  | 53.4                                | + 0.9                                  | 0.0081           | 1.28                   | 0.15                                |                 |
| 6.   | Neurofibroma of the stomach..... | 47.5           | 8                  | 58.1                                | 7.17            | 0.46       | 61.9  | 53.7                                | + 8.2                                  | 0.0084           | 1.28                   | 0.15                                |                 |
| 7.   | Pancreatic fistula.....          | 41.4           | 6                  | 56.2                                | 7.03            | 0.45       | 44.9  | 62.16                               | -17.2                                  | -0.0692          | 1.42                   | 0.17                                |                 |
| 8.   | Carcinoma of the rectum.....     | 55             | 10                 | 60                                  | 7.50            | 0.48       | 63.8  | 38.51                               | +25.3                                  | 0.0033           | 1.14                   | 0.14                                |                 |
| 9.   | Varicose ulcer.....              | 58.5           | 10                 | 60                                  | 7.50            | 0.48       | 70.8  | 59.2                                | +11.6                                  | 0.0506           | 1.07                   | 0.13                                |                 |
| 10.  | Varicose ulcer.....              | 90             | 9                  | 60                                  | 7.50            | 0.48       | 71.8  | 80.4                                | - 8.6                                  | -0.0106          | 0.70                   | 0.08                                |                 |
| 11.  | Varicose ulcer.....              | 90             | 4                  | 30                                  | 11.25           | 0.72       | 47.9  | 39.6                                | + 8.3                                  | 0.0231           | 1.05                   | 0.13                                |                 |

TABLE 4.—*Nitrogen Balance Studies with Large Amounts of Essensamine*

| Case         | Diagnosis                        | Weight,<br>Kg. | Days<br>on<br>Diet | Average Daily<br>Essensamine Intake |                 |                 | Average<br>Daily Addi-<br>tional<br>Nitrogen<br>Intake | Total<br>Nitrogen<br>Intake,<br>Gm. | Total<br>Nitrogen<br>Excretion,<br>Gm. | Nitrogen Balance |         | Daily Intake per Kg.<br>Body Weight |                 |
|--------------|----------------------------------|----------------|--------------------|-------------------------------------|-----------------|-----------------|--|-------------------------------------|--|------------------|---------|-------------------------------------|-----------------|
|              |                                  |                |                    | Gm.<br>Protein                      | Gm.<br>Nitrogen | Gm.<br>Nitrogen |  |                                     |  | Total            | Per Day | Gm.<br>Protein                      | Gm.<br>Nitrogen |
|              |                                  |                |                    |                                     |                 |                 |  |                                     |  |                  |         |                                     |                 |
| 1.           | Gastritis.....                   | 62.7           | 7                  | 180                                 | 22.5            | 7.5             | 209.8  | 155.2                               | + 54.6                                 | 7.8              | 4.30    | 0.48                                |                 |
| 3.           | Carcinoma of the sigmoid.....    | 49             | 26                 | 150                                 | 18.75           | 8.0             | 698.0  | 449.8                               | +248.2                                 | 9.5              | 4.08    | 0.54                                |                 |
| 4.           | Pelvic inflammatory disease..... | 49             | 18                 | 155                                 | 19.45           | 7.4             | 484.0  | 375                                 | +109                                   | 6.6              | 4.15    | 0.54                                |                 |
| 5.           | Carcinoma of the rectum.....     | 40             | 15                 | 118                                 | 14.7            | 7.25            | 330  | 116.0                               | +214.0                                 | 14.3             | 4.07    | 0.55                                |                 |
| 6.           | Neurofibroma of the stomach..... | 47.5           | 20                 | 136                                 | 17.0            | 9.9             | 538  | 341.3                               | +196.7                                 | 9.8              | 4.12    | 0.56                                |                 |
| 7.           | Pancreatic fistula.....          | 41.4           | 20                 | 144                                 | 18.0            | 9.0             | 542.2  | 317.0                               | +225.2                                 | 11.3             | 4.80    | 0.65                                |                 |
| 9.           | Varicose ulcer.....              | 54             | 10                 | 170                                 | 21.25           | 15.7            | 369.0  | 195.7                               | +173.3                                 | 17.3             | 4.9     | 0.68                                |                 |
| 10.          | Varicose ulcer.....              | 58.5           | 10                 | 170                                 | 21.25           | 15.5            | 387.5  | 199.8                               | +207.7                                 | 20.8             | 4.5     | 0.62                                |                 |
| 11.          | Varicose ulcer.....              | 90             | 9                  | 168                                 | 20.8            | 10.9            | 286.5  | 216                                 | + 70.5                                 | 7.8              | 2.6     | 0.35                                |                 |
| *12.         | Empyema.....                     | 53             | 17                 | 219                                 | 20.8            | 3.1             | 415.4  | 229                                 | +186.4                                 | 11.0             | 2.9     | 0.41                                |                 |
| *13.         | Burn.....                        | 53             | 18                 | 223                                 | 21.2            | 3.0             | 436.0  | 175.7                               | +260.3                                 | 13.9             | 4.55    | 0.45                                |                 |
| *14.         | Empyema.....                     | 62.5           | 18                 | 283                                 | 28.3            | 3.7             | 602.7  | 289.7                               | +313.0                                 | 17.4             | 4.89    | 0.51                                |                 |
| Average..... |                                  |                |                    |                                     |                 |                 |  |                                     |  | .....            | 4.25    | 0.52                                |                 |

\* The preparation of Essensamine given in cases listed here contained 10 Gm. of sodium chloride and 9.5 Gm. of nitrogen per hundred grams; all other preparations contained 1.5 Gm. of sodium chloride and 12.5 Gm. of nitrogen per hundred grams.

which were acceptable. The material also could be incorporated in cereals and vegetables. The latter were vehicles for the Essenamine with the high salt content for 3 subjects (cases 12, 13 and 14 in table 4). The exact composition of the prepared foods is given in the appendix. The caloric intake varied between 2,500 and 3,000 calories. Maintenance doses of vitamins B and C were provided for, in experiments both with the high and with the low Essenamine content, as adjuvant medication.

#### RESULTS

*Minimal Essenamine Requirements.*—The 11 subjects placed on the minimal diet ingested from 48.7 to 90 Gm. of Essenamine daily, or from 5.86 to 11.25 Gm. of Essenamine nitrogen daily (see table 3). The additional nitrogen intake was usually of the order of 0.5 Gm. Positive nitrogen balance was achieved in ten of the experiments. The nitrogen per kilogram per day required for this achievement ranged from 0.13 to 0.16 Gm. per day. Patient 11, who weighed 90 Kg., was unable to achieve positive nitrogen balance on 0.08 Gm. per kilogram per day but did so on 0.13 Gm.

Patient 7 failed to show a positive nitrogen balance during the six days of study, in spite of an intake of 0.17 Gm. per kilogram per day. This patient had been extremely ill just previous to the experimental study. She had a pancreatic fistula and had suffered from severe dehydration and extrarenal azotemia. Parenterally injected fluids had lowered the blood nonprotein nitrogen level from 131 to 50 mg. per hundred cubic centimeters and had raised the plasma volume from 1,450 to 2,030 cc. It was at this stage that the nitrogen balance study was begun. It was not improbable that some of the excreted nitrogen represented previously retained nonprotein nitrogen. At any rate, since the results from this patient are completely at variance with those from the others, they should probably be discarded in the evaluation of the minimal requirements for nitrogen balance.

The average daily nitrogen intake in the ten experiments in which positive nitrogen balance was achieved was 0.145 Gm. per kilogram per day. In these ten experiments the average positive nitrogen balance was 11.85 Gm. per person, or 0.0249 Gm. per kilogram per day. To determine the average daily Essenamine nitrogen requirement for exact nitrogen balance, it is necessary to know the slope of the curve relating nitrogen intake to nitrogen balance, which Allison<sup>10</sup> has shown to be a straight line near the region of zero nitrogen balance. Unfortunately, the experiments were not designed to show such a slope. Balances at various levels of nitrogen intake were not determined except in case 11. In this case there were two levels of intake. If one plots, as in chart 1, the two points of the experiment and draws a line between them, then the remaining nine points similarly plotted will be found to fall reasonably well on either side of this line. The average for the ten experiments with positive nitrogen balance, represented by X in chart 1, falls near

the sloping line. If it is assumed that the line drawn for case 11 has the average slope for all the 10 patients with positive nitrogen balance, then another line drawn through *X* parallel to this line will pass through the base line of zero nitrogen balance at the point defining the average intake required for exact nitrogen balance. This point is slightly less than 0.11 Gm. per kilogram per day. Even if these assumptions are unwarranted, the calculation based on them gives some notion of the average intake required and it is reasonably certain that it is

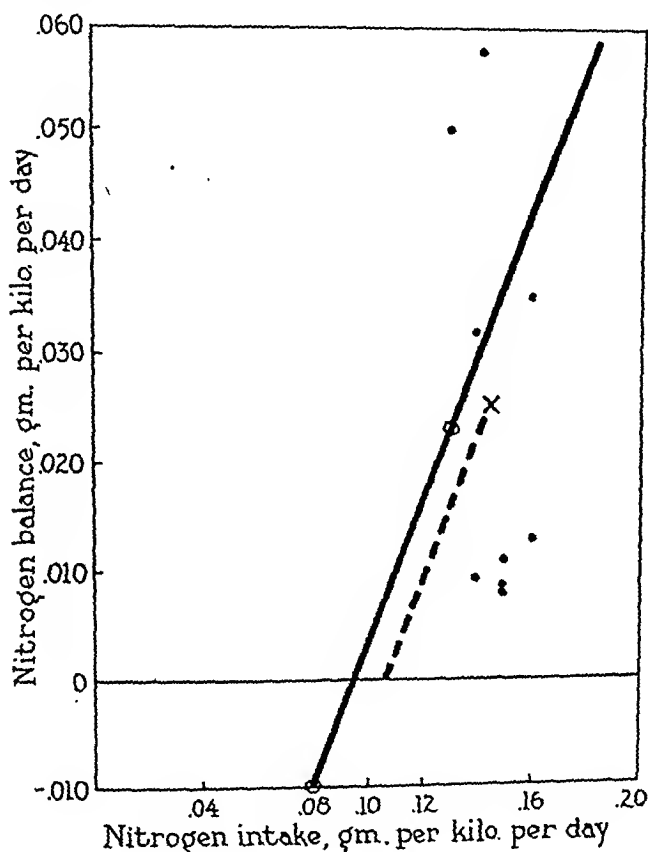


Chart 1.—The relation of nitrogen balance to nitrogen intake at low levels. The solid black line represents two levels of intake in 1 patient (one with negative balance and one with positive). The points representing the results in 9 other subjects with positive nitrogen balance fall on both sides of this line. The average for all ten experiments is represented by *X*. The line through *X* parallel to the solid line intersects the zero balance line at the level of average intake for exact nitrogen balance, a little less than 0.11 Gm. per kilogram per day.

appreciably less than the 0.145 Gm. per kilogram required for the moderately positive nitrogen balance of these experiments.

*High Essenamaine Diets.*—The experiments were originally designed to determine the upper limits of protein intake attainable with the preparation used, but it was soon recognized that for a number of patients this would involve the frequent rejection of part of the food

offered. Since the measurement of such unused food makes for considerable error in the determination of nitrogen balance, it was decided to stay within the limits imposed by the patients, who for the most part had no conception of the nature of the experiment. It was possible even in these circumstances to accomplish the ingestion in 12 out of 14 cases of more than 0.45 Gm. nitrogen per kilogram per day, or about four times the estimated minimal requirements (see table 4).

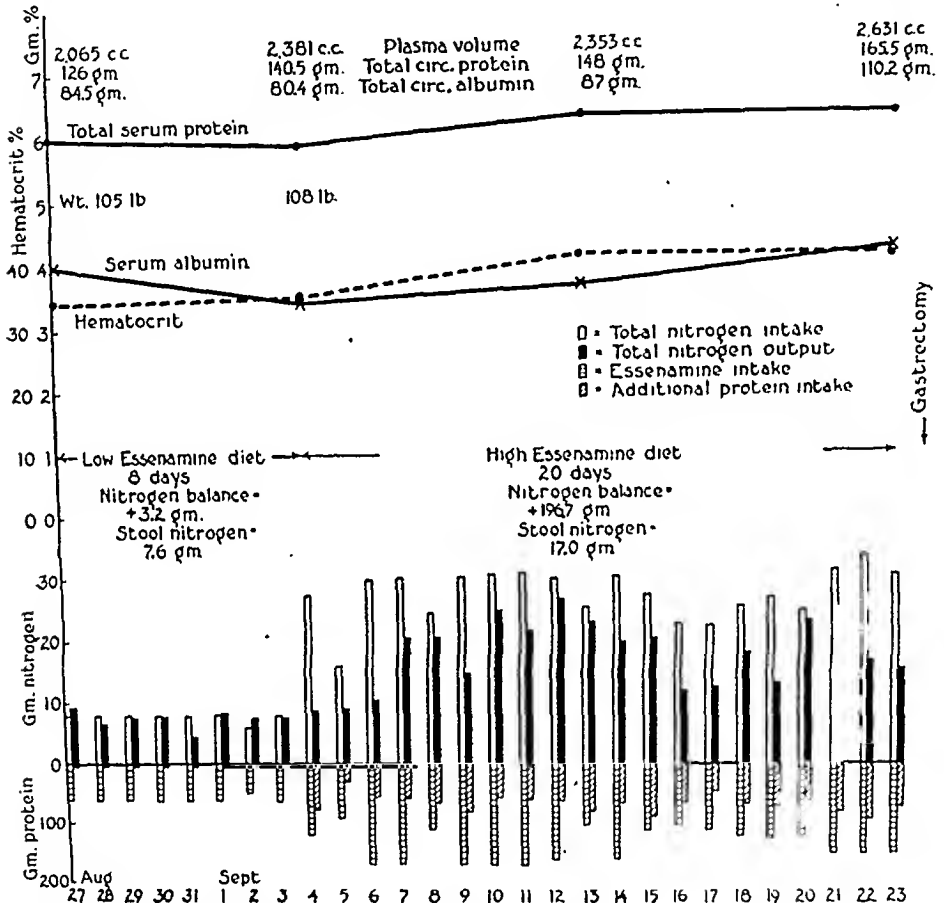


Chart 2.—Daily nitrogen balance record, with Essenamine as the principal source of protein given orally, of a 56 year old patient with neurofibroma of the stomach prepared for a transthoracic gastrectomy. On the low Essenamine diet the patient retained 5.4 per cent of the ingested nitrogen; on the high Essenamine diet this patient retained 36.5 per cent. There was a progressive increase in the plasma volume, total circulating protein and albumin in addition to a 7 pound (3.2 Kg.) gain in weight and general definite clinical improvement (case 6).

In all twelve experiments there was large retention of nitrogen, ranging from 6 to 20 Gm. daily, with an average of 12 Gm. per day. In all cases, too, there was an increased sense of well-being, gain in weight and strength and a steady improvement in appetite. There was no

elevation of nonprotein nitrogen above normal limits. The daily courses in three of the experiments are shown in charts 2, 3 and 4.

Comparison of the distribution of the absorbed nitrogen in the minimal and in the high protein diet (as seen in table 5) shows that there

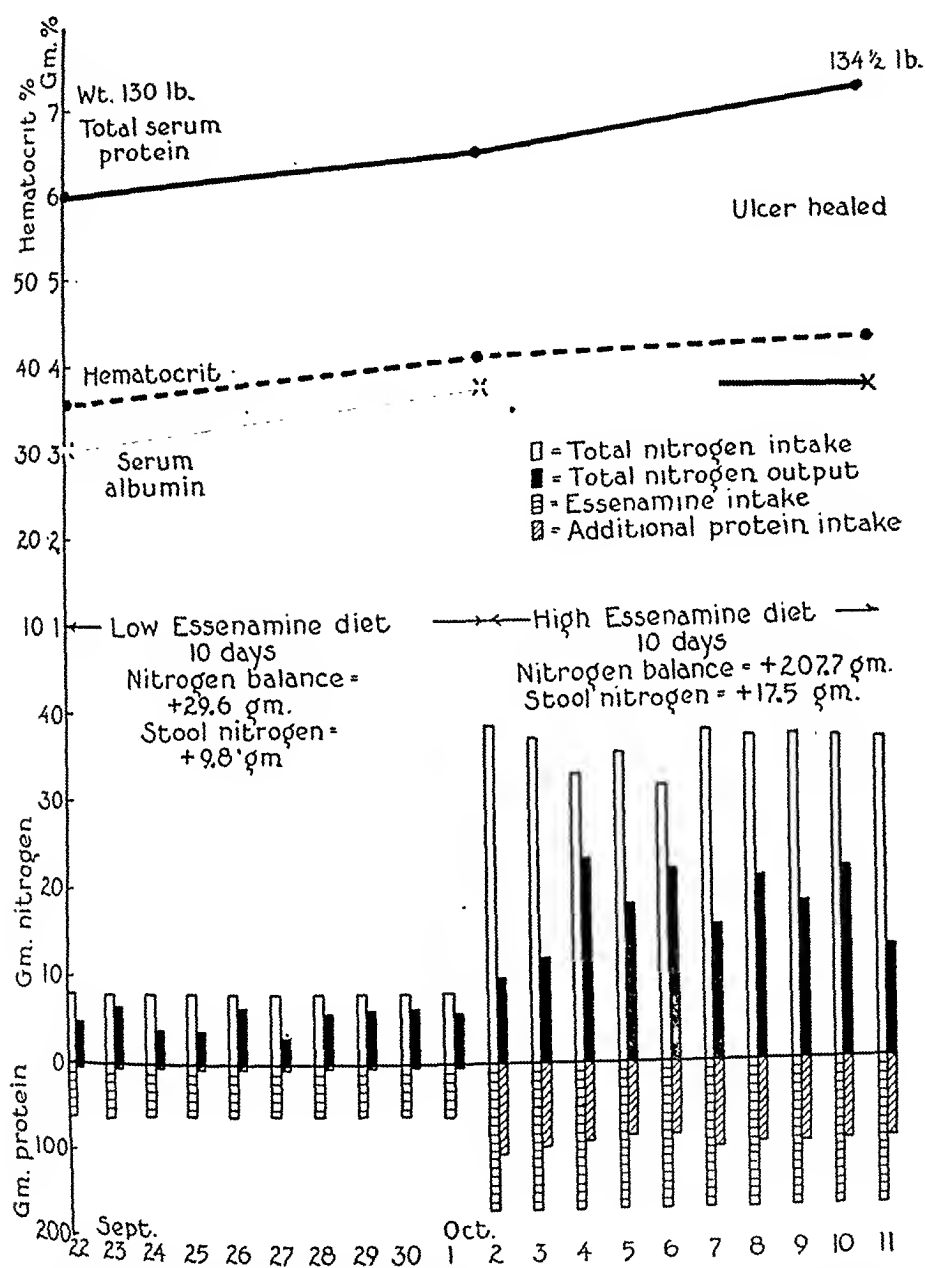


Chart 3.—Daily nitrogen balance studies in a 41 year old patient with alcoholic malnutrition and delayed healing of varicose ulcer. A substantial positive nitrogen balance occurred with both the low and the high Essenamine diet. The total serum protein content rose from 5.96 to 7.01 Gm. per hundred cubic centimeters, while the serum albumin level rose from 3.08 to 3.58 Gm. per hundred cubic centimeters. Gain in weight and improvement in wound healing and clinical appearance corresponded with these findings (case 10).

was little increase in fecal nitrogen on the high protein diet. The average daily fecal nitrogen for the low protein diet was 1.03 Gm., and for the high protein diet it was 1.47 Gm. This finding indicates the high degree of digestibility (and absorbability) of the proteins fed. The coefficient of digestibility for the total protein fed on the high Essenamine diet was 0.95, that is, 5 per cent of the ingested nitrogen

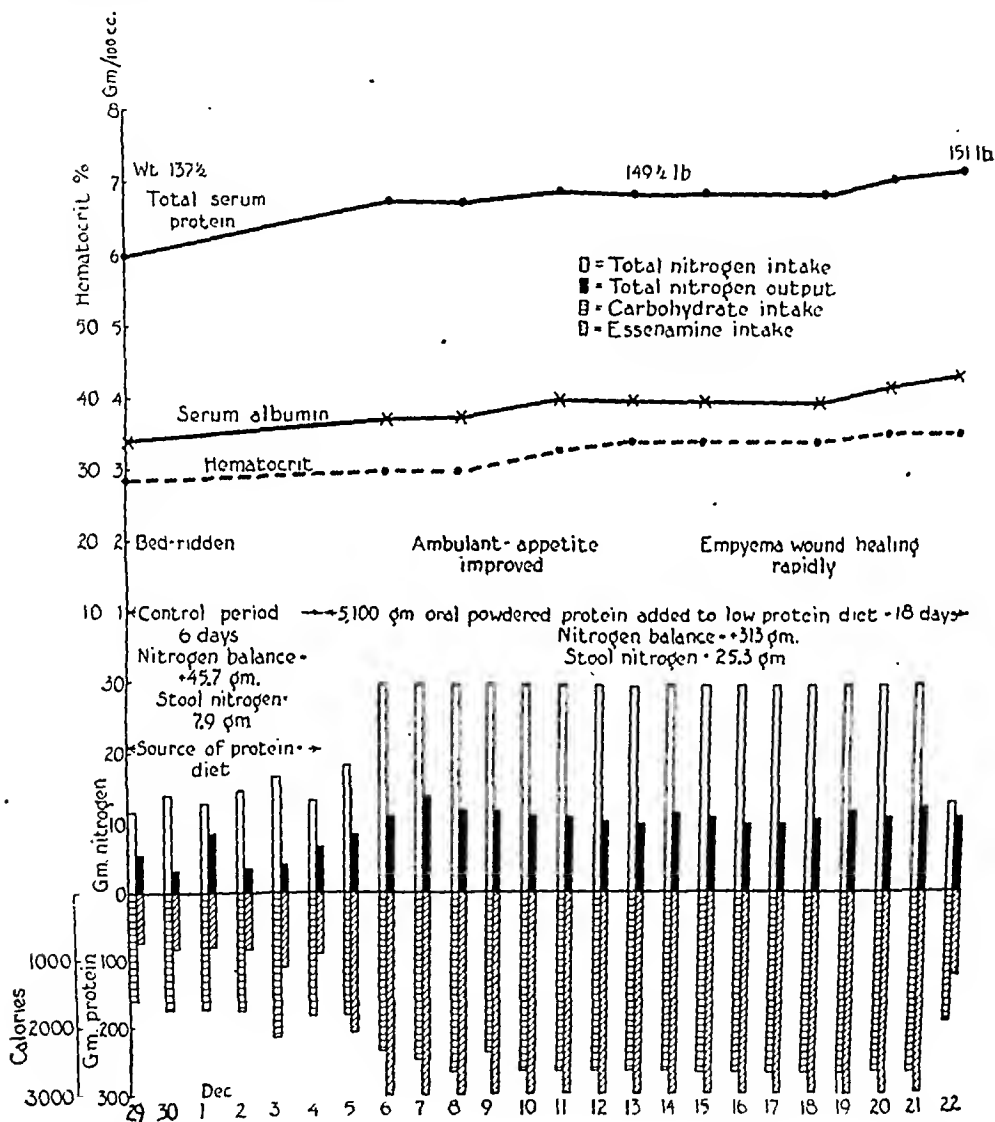


Chart 4. —Daily nitrogen balance studies, with Essenamine as the principal source of protein given orally, on a 28 year old patient with empyema of the chest who ingested 300 Gm. of protein daily for seventeen days. This particular form of Essenamine contained 9.5 Gm. of nitrogen and 10 Gm. of sodium chloride per hundred grams. The patient retained 51.8 per cent of the ingested nitrogen. This was associated with a 13 1/2 pound (6.1 Kg.) gain in weight and an increased urinary output. The total serum protein content rose from 5.97 Gm. per hundred cubic centimeters to 7.23 Gm. per hundred cubic centimeters and the serum albumin level from 3.4 to 4.34 Gm. per hundred cubic centimeters (case 14).

was found in the feces. Since the coefficient of digestibility of casein is rated at 0.96 and that of vegetable and cereal proteins somewhat lower, then the digestibility of Essenamnine is on the same order as that of casein. Such a finding is especially significant in that Essenamnine has a limited solubility. A good portion of it might have been expected to pass through the bowel unabsorbed.

On the high protein diet the small absolute increase in fecal nitrogen lowered the percentage of total nitrogen in the feces from 11.8 to 5.0 per cent. Similarly, the urinary nitrogen on the high protein diet,

TABLE 5.—*Fate of Nitrogen Ingested in Essenamnine Diet*

| Case No.     | Essenamnine Diet | Nitrogen Ingested, Gm. | Excreted in Urine, per Cent | Stool Excretion      |          | Retained, per Cent |
|--------------|------------------|------------------------|-----------------------------|----------------------|----------|--------------------|
|              |                  |                        |                             | Gm. Nitrogen per Day | Per Cent |                    |
| 1.....       | Low              | 67.7                   | 76.2                        | 1.71                 | 16.2     | 7.6                |
|              | High             | 209.8                  | 65.3                        | 2.54                 | 8.5      | 26.2               |
| 2.....       | Low              | 79.1                   | 63.2                        | 1.39                 | 14.1     | 22.7               |
|              | High             | 698.0                  | 57.5                        | 1.83                 | 6.8      | 35.8               |
| 3.....       | Low              | 71.8                   | 66.7                        | 0.94                 | 11.8     | 21.5               |
|              | High             | 484.0                  | 66.6                        | 2.55                 | 9.5      | 23.9               |
| 4.....       | Low              | 50.3                   | 57.0                        | 0.49                 | 7.8      | 5.2                |
|              | High             | 330.0                  | 31.5                        | 1.03                 | 4.7      | 63.8               |
| 5.....       | Low              | 61.9                   | 82.4                        | 0.94                 | 12.2     | 5.4                |
|              | High             | 538.0                  | 60.4                        | 0.83                 | 3.1      | 36.5               |
| 6.....       | Low              | 44.9                   | 135.0*                      | 0.21                 | 2.87     | -37.8*             |
|              | High             | 542.2                  | 53.2                        | 1.53                 | 4.9      | 41.9               |
| 7.....       | Low              | 63.6                   | 34.0                        | 2.09                 | 26.3     | 39.7               |
|              | High             | 79.8                   | 85.8                        | 0.63                 | 7.9      | 0.3                |
| 8.....       | Low              | 369.0                  | 48.6                        | 1.62                 | 4.4      | 47.0               |
|              | High             | 79.8                   | 50.6                        | 0.97                 | 12.2     | 37.2               |
| 9.....       | Low              | 367.5                  | 38.7                        | 1.73                 | 4.7      | 56.6               |
|              | High             | 71.8                   | 96.7                        | 1.21                 | 15.2     | -11.2*             |
| 10.....      | Low              | 47.2                   | 74.0                        | 1.17                 | 9.9      | 16.1               |
|              | High             | 286.5                  | 71.8                        | 1.21                 | 3.8      | 24.4               |
| 11.....      | Low              | 415.4                  | 52.1                        | 0.93                 | 3.8      | 44.1               |
|              | High             | 436.0                  | 37.6                        | 0.61                 | 2.5      | 59.9               |
| 12.....      | Low              | 602.7                  | 44.1                        | 1.37                 | 4.1      | 51.8               |
|              | High             | .....                  | 52.2                        | 1.47                 | 5.0      | 42.0               |
| Average..... | Low              | .....                  | 78.05                       | 1.03                 | 11.8     | 11.7               |
|              | High             | .....                  | 52.2                        | 1.47                 | 5.0      | 42.0               |

\* Negative nitrogen balance.

though increased absolutely, diminished relatively, the percentage of total nitrogen intake dropping from 78 per cent to 52.2 per cent. Thus the percentile retention of nitrogen increased from 11 per cent on the low protein diet to 43 per cent on the high protein diet. In other words, nearly half of the ingested nitrogen was retained by these subjects. These results are in sharp contrast to the 23 per cent retention of the intravenously injected nitrogen when maximal quantities were administered.<sup>1</sup>

*Systemic Effects of the High Protein Diet.*—As has been stated, the large retention of nitrogen in protein-deficient subjects as shown even in those relatively brief experiments was reflected in an increased



sense of well-being, improvement in appetite and usually a moderate gain in weight. Some of these improvements occurred even when the subjects were on the maintenance diet. Here they may have meant chiefly a restoration of water and mineral balance. This was supported by the fact that the hematocrit level was usually lower at the end of the maintenance period than at the start of the experiment. On the high protein diet, the gain in weight usually continued and was in many cases a genuine gain in flesh, for in this period the hematocrit values usually increased.

Table 6 shows the effect of the dietary regimen on the weight, hematocrit level, serum protein content and plasma volume for all the experiments. (Determinations of plasma volume were made in only eight experiments.) The early fall in hematocrit values was paralleled by a drop in serum protein concentration, the two being consequences of hemodilution. Estimations of plasma volume confirmed this trend, but the increase in plasma volume was not necessarily on the same order as the rise in hematocrit content. This phenomenon has been well demonstrated by Abbott and Mellors.<sup>11</sup> On the high protein diet, the serum protein concentration rose in 9 cases and decreased in 3. Of the latter, only 1 case represented a decrease in albumin concentration. In case 4 a drop in serum protein concentration actually represented a fall in an abnormally high concentration of serum globulin to normal during the period of study. This was a case of chronic pelvic inflammatory disease. In the 8 cases in which estimations of plasma volume were made, the improvement in serum protein production, especially that of serum albumin, could be better recognized by a study of the total circulating proteins. In all eight experiments there was a rise in total circulating albumin. In 6 of the 8 cases, the rise was considerable.

#### COMMENT

Though the need for a high protein diet to combat the effects of low concentrations of serum protein and their accompanying deficiency of tissue protein have been recognized since 1917, when Epstein<sup>12</sup> recommended such diets for the treatment of nephrosis, the difficulties of achieving satisfactory high protein alimentation have never been overcome. A sick patient can seldom be forced to eat a natural diet containing more than 100 Gm. of protein for any extended period, whether the chief source of protein is meat, milk or cheese. The bulk is too great, and the sense of fulness and satiation is overwhelming. It is necessary to add protein or its equivalent in a concentrated form.

11. Abbott, W. E., and Mellors, R. C.: Total Circulating Plasma Proteins in Surgical Patients with Dehydration and Malnutrition, *Arch. Surg.* **46**:277 (Feb.) 1943.

12. Epstein, A. A.: Concerning the Causation of Edema in Chronic Parenchymatous Nephritis: Method for Its Alleviation, *Am. J. M. Sc.* **154**:638, 1917.

TABLE 6.—Effect of Essenammine Diets on Circulating Proteins

| Case No. | Essenammine Diet | Initial Weight, Kg. | Weight Gain, Kg. | Nitrogen Balance, Gm. | Hematocrit Level, per Cent | Total Protein, Gm. per 100 Cc. | Albumin, Gm. per 100 Cc. | Plasma Volume, Cc. | Total Circulating Protein, Gm. | Total Circulating Albumin, Gm. |
|----------|------------------|---------------------|------------------|-----------------------|----------------------------|--------------------------------|--------------------------|--------------------|--------------------------------|--------------------------------|
| 1        | Control.....     | 62.7                | ...              | .....                 | 46                         | 6.35                           | 3.76                     | 2,500              | 158.5                          | 94.0                           |
|          | Low.....         | ...                 | 0.3              | + 8.5                 | 40.5                       | 6.82                           | 4.07                     | 2,083              | 132.6                          | 84.5                           |
|          | High.....        | ...                 | 1.3              | + 54.6                | 49                         | 6.95                           | 4.41                     | 3,030              | 201.8                          | 133.1                          |
| 2        | Control.....     | 70                  | ...              | .....                 | 45                         | 5.31                           | 3.50                     | 2,857              | 151.7                          | 99.8                           |
|          | Low.....         | ...                 | 0                | + 17.5                | 42                         | 5.60                           | 3.51                     | 3,175              | 177.5                          | 111.5                          |
| 3        | Control.....     | 49                  | ...              | .....                 | 45                         | 6.28                           | 4.35                     | 1,808              | 113.4                          | 78.0                           |
|          | Low.....         | ...                 | 0                | + 15.4                | 40.5                       | 5.86                           | 3.87                     | 1,751              | 102.4                          | 63.8                           |
|          | High.....        | ...                 | 1.5              | + 47.2                | 46.5                       | 7.01                           | 4.84                     | 2,128              | 149.8                          | 103.2                          |
| 4        | Control.....     | 49                  | ...              | .....                 | 40                         | 8.12                           | 4.09                     | 2,817              | 228.4                          | 115.3                          |
|          | Low.....         | ...                 | 0                | + 5.8                 | 36                         | 7.50                           | 4.16                     | 2,565              | 195.6                          | 107.6                          |
|          | High.....        | ...                 | 1.2              | +109.0                | 36.5                       | 7.13                           | 4.33                     | 2,703              | 193.2                          | 117.0                          |
| 5        | Control.....     | 40                  | ...              | .....                 | 39.5                       | 6.33                           | 3.83                     | 2,456              | 155.4                          | 93.8                           |
|          | Low.....         | ...                 | 0                | + 2.9                 | 32                         | 6.54                           | 4.00                     | 2,300              | 150.5                          | 105.7                          |
|          | High.....        | ...                 | 5                | +214.0                | 43                         | 7.10                           | 4.30                     | 2,632              | 187.0                          | 113.2                          |
| 6        | Control.....     | 47.5                | ...              | .....                 | 34                         | 6.08                           | 4.05                     | 2,663              | 196.0                          | 84.5                           |
|          | Low.....         | ...                 | 1.2              | + 3.2                 | 35                         | 5.80                           | 3.37                     | 2,381              | 140.5                          | 80.4                           |
|          | High.....        | ...                 | 1.8              | +196.7                | 41                         | 6.29                           | 4.19                     | 2,631              | 165.5                          | 110.2                          |
| 7        | Control.....     | 41.4                | ...              | .....                 | 52                         | 6.65                           | 3.84                     | 2,083              | 139.6                          | 80.0                           |
|          | Low.....         | ...                 | 6.3              | - 17.2                | 46.5                       | 6.71                           | 4.05                     | 2,298              | 155.0                          | 92.9                           |
|          | High.....        | ...                 | 2.7              | +225.0                | 40                         | 6.31                           | 4.51                     | 2,865              | 180.5                          | 131.2                          |
| 8        | Control.....     | 55                  | ...              | .....                 | 48                         | 5.65                           | 3.25                     | 2,000              | 113.2                          | 65.0                           |
|          | Low.....         | ...                 | 0.9              | + 25.3                | 39                         | 6.28                           | 4.18                     | 2,353              | 148.0                          | 99.2                           |
| 9        | Control.....     | 54                  | ...              | .....                 | 45                         | 6.43                           | 2.93                     | ...                | ...                            | ...                            |
|          | Low.....         | ...                 | 2.0              | + 5.0                 | 47                         | 6.59                           | 2.99                     | ...                | ...                            | ...                            |
|          | High.....        | ...                 | 0.6              | +173.3                | 43                         | 6.73                           | 3.04                     | ...                | ...                            | ...                            |
| 10       | Control.....     | 58.5                | ...              | .....                 | 35.5                       | 5.96                           | 3.08                     | ...                | ...                            | ...                            |
|          | Low.....         | ...                 | 1.3              | + 29.6                | 40                         | 6.36                           | 3.65                     | ...                | ...                            | ...                            |
|          | High.....        | ...                 | 0.6              | +207.7                | 41.5                       | 7.01                           | 2.58                     | ...                | ...                            | ...                            |
| 11       | Control.....     | 90                  | ...              | .....                 | 51                         | 6.52                           | 4.18                     | ...                | ...                            | ...                            |
|          | Low.....         | ...                 | 0                | + 8.6                 | 49                         | 6.12                           | 4.37                     | ...                | ...                            | ...                            |
|          | High.....        | ...                 | 0.9              | + 70.5                | 48                         | 7.11                           | 5.23                     | ...                | ...                            | ...                            |
| 12       | Control.....     | 58                  | ...              | .....                 | 37                         | 7.13                           | 2.60                     | ...                | ...                            | ...                            |
|          | High.....        | ...                 | 1.5              | +186.4                | 31.5                       | 6.98                           | 3.23                     | ...                | ...                            | ...                            |
| 13       | Control.....     | 83                  | ...              | .....                 | 31                         | 5.83                           | 3.88                     | ...                | ...                            | ...                            |
|          | High.....        | ...                 | 1.2              | +249.7                | 31.5                       | 6.12                           | 3.72                     | ...                | ...                            | ...                            |
| 14       | Control.....     | 62.5                | ...              | .....                 | 28.5                       | 5.97                           | 3.41                     | ...                | ...                            | ...                            |
|          | High.....        | ...                 | 6.3              | +313.0                | 36.5                       | 7.23                           | 4.34                     | ...                | ...                            | ...                            |

The use of such products as dried skim milk, soya protein, peanut flour, dried brewers' yeast and wheat or corn germ has recently been discussed by Turner.<sup>13</sup> Even when these products are incorporated as dry products in the daily food items, it has been difficult to get above 150 Gm. of protein daily, because all these items usually contain less than 50 per cent protein and because they have a pronounced taste, which though not unpleasant becomes monotonous and tiresome.

The use of protein digests for oral alimentation has to date proved disappointing. Hydrolysates of protein, whether prepared by enzyme or by acid, have a bad taste that eventually proves nauseating. A patient may be persuaded to take some in a disguised form for a few days, but long before a demonstrable nutritional effect can be produced he will usually have rebelled at a continuance of this regimen. In such cases feeding by intranasal tube may be resorted to, and, as has been stated, this can at times be successful. But most often such feeding defeats its own purpose by destroying whatever vestige is left of the appetite for normal foods.

Our success with the employment of Essenamine as the principal ingredient of a high protein diet was probably due to four factors: (1) its high concentration of proteins (with 12.5 per cent nitrogen, its protein content can be regarded as 81.3 per cent, if Essenamine has the same nitrogen factor of 6.5 that lactalbumin has<sup>14</sup>); (2) its high content of essential amino acids, that is, its high biologic value as indicated from the fact that about 0.11 Gm. of nitrogen per kilogram per day were required in our experiment for nitrogen balance; (3) its lack of any pronounced taste, so that it can be incorporated in large quantities in other foods that have a pleasant taste, and (4) its limited solubility. The last of these qualities could not have been anticipated as being a virtue. It had been feared that the relative insolubility would limit the digestibility and absorbability of the protein. But this did not prove to be the case, as shown by the low content of fecal nitrogen. On the other hand, the limited solubility apparently minimized the concentration of amino acids in the small intestine at any one time, so that the sense of fulness was postponed and the tendency to diarrhea, which has been frequently present in intubation feedings of protein hydrolysates, did not occur.

For the purpose of simplicity in the management of the nitrogen balance experiments, the number of foods in which Essenamine was incorporated was small, but for other patients, for whom no balance

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13. Turner, D. F.: Selection of Protein Containing Foods to Meet Protein Requirements, *J. A. M. A.* **128**:590 (June 23) 1945.

14. Jones, D. B.: Factors for Converting Percentages of Nitrogen in Foods and Feeds into Percentages of Protein, Circular no. 183, United States Department of Agriculture, 1931.

studies were carried out, Essenamaine was incorporated in tasty preparations of many foods. These include bread, cookies, candies, sandwich spreads, meat sauces, vegetable sauces, cereals, fruit crisps, puddings, custards and milk drinks. Such a variety of dishes is of particular value in the home management of protein deficiency, where special care and individual attention may be devoted to the needs and tastes of the patient. Even in the hospital, many of these dishes can be prepared without any great extension of the activities of the dietetic department. In the simplest form, the protein can be suspended in milk or orange juice immediately before being administered.

In the experiments with the minimal Essenamaine requirements, the limitations imposed by the experiment made for a monotonous diet, so that it could not be protracted for any long period. But in the high protein diets, the menus offered were regarded as satisfactory by the patients and could have been continued for a longer period than the actual duration of the experiments. It was the rigor of the nitrogen balance regimen that determined the length of the experiment.

There was no recognizable correlation of the quantity of nitrogen retained per day with the initial concentrations of serum protein or with the rise of serum protein concentration to normal limits, though such correlations might have been expected. Possibly this was due to the fact that none of the patients had extremely low levels of serum protein. Also there was no indication of a tapering of the amount of positive nitrogen balance as the experiments progressed (charts 2, 3 and 4), even though in a number of cases the serum protein concentration had apparently returned to normal values. This finding might mean either that the serum protein concentration could return to normal before the body stores of protein had been fully repleted or that nitrogen compounds might be temporarily stored beyond the body needs. The former explanation was more likely to be the correct one, especially since the clinical appearance of the patients and their relatively small gain in weight implied that they were far from restored to normal condition during the period of the experiments.

The actual time required for complete restitution of body protein stores with our high protein regimen could not be determined from the experiments. However, it can be pointed out that in the several cases in which these experiments preceded surgical treatment the patients underwent the operation well and had good postoperative courses. Also the patients who were placed on this diet postoperatively convalesced rapidly and without complications.

#### SUMMARY AND CONCLUSIONS

1. Fourteen surgical patients were studied in nitrogen balance experiments to determine the clinical effectiveness of Essenamaine, a

new processed protein derivative of lactalbumin, as a high protein therapeutic agent.

2. In ten of eleven experiments to determine the minimal nitrogen requirement of Essenamine for nitrogen balance, positive nitrogen balance was achieved with an intake of 0.145 Gm. of nitrogen per kilogram per day. For exact nitrogen balance, it was estimated that 0.11 Gm. per kilogram per day would be required.

3. On the minimal intake of Essenamine, 78 per cent of the ingested nitrogen was excreted in the urine, 11 per cent was excreted in the feces and 11 per cent was retained in the body.

4. In twelve balance experiments in which Essenamine was used as the main ingredient of a high protein diet for periods ranging from seven to twenty-six days, 0.52 Gm. of nitrogen per kilogram per day was given orally. This diet produced positive nitrogen balances ranging from 6 to 20 Gm. of nitrogen per day, with an average of 12 Gm.

5. On the high Essenamine intake, 52.2 per cent of the ingested nitrogen was excreted in the urine, 5 per cent was excreted in the feces and 42.8 per cent was retained, indicating the high digestibility and the high biologic value of proteins ingested.

6. Both the maintenance and the high protein diet usually produced increases in body weight plasma volume, serum protein and serum albumin concentrations and total circulating albumin, but there was no good correlation between these responses and the amount of positive nitrogen balance.

7. Essenamine can easily be incorporated in a large variety of liquid and solid foods to make palatable preparations. Its use as a means of producing a high protein diet is a practical procedure, which has none of the limitations of parenteral or intubation therapy.

## APPENDIX

### I. Diet for minimal intake of Essenamine for nitrogen balance

#### A. Menu

##### 1. Breakfast

Orange

Essenamine drink (5 Gm. of Essenamine)

Essenamine custard (5 Gm. of Essenamine)

Hot tea

##### 2. Lunch

Vegetable puree (7.5 Gm. of Essenamine)

Fruit crisp (7.5 Gm. of Essenamine)

Essenamine drink (10 Gm. of Essenamine)

##### 3. Supper

Vegetable puree (7.5 Gm. of Essenamine)

Fruit crisp (7.5 Gm. of Essenamine)

Essenamine drink (10 Gm. of Essenamine)

Total Essenamine 60 Gm.  
 Total calories about 2,100.  
 Carbohydrate 260 Gm. (approximately), protein 60 Gm. and fat 90 Gm.

## B. Recipes

## 1. Custard and drink (for one day)

|                      |                             |
|----------------------|-----------------------------|
| 25 Gm. tapioca flour | 30 Gm. Essenamine           |
| 25 Gm. sugar         | 80 Gm. corn syrup           |
| 30 Gm. vegetable oil | 3 Gm. agar                  |
| 1 Gm. salt           | 3 teaspoons vanilla extract |
| 1 Gm. cinnamon       | 250 cc. water               |
| Pinch of nutmeg      |                             |

Mix all ingredients except agar. Cook until thick, add agar, mix in high speed blender and cool in refrigerator. For drink add additional 150 cc. of water.

## 2. Vegetable sauce (for one day)

|   |                                    |
|---|------------------------------------|
| 30 Gm. vegetable oil                          | 20 Gm. corn syrup                  |
| 15 Gm. tapioca flour                          | 2 Gm. salt                         |
| 15 Gm. Essenamine                             | $\frac{1}{4}$ teaspoon celery salt |
| $\frac{1}{4}$ teaspoon chopped parsley leaves | $\frac{1}{4}$ teaspoon onion salt  |
|   | 75 cc. water                       |

Mix thoroughly, and cook over medium flame until thick. Cool.

## 3. Fruit crisp (three servings for one day)

|                     |                     |
|---------------------|---------------------|
| 200 Gm. fruit       | 100 Gm. brown sugar |
| 5 Gm. tapioca flour | 15 Gm. Essenamine   |
| 2 Gm. salt          | 1 Gm. cinnamon      |
| 30 Gm. oil          | Pinch of nutmeg     |
|                     | Water if necessary  |

Mix until crumbly. Line a baking pan with some of fruit. Add mixture. Bake in a moderate oven until brown. Divide into three servings.

## Diets for high Essenamine intake

## A. Low residue diet plus 150 Gm. of Essenamine in 1,500 cc. of milk drink

## 1. Menu

| Breakfast      | Lunch                 | Dinner                    |
|----------------|-----------------------|---------------------------|
| Fruit          | Egg or meat or cheese | Soup                      |
| Cereal or eggs | Potatoes              | Cheese                    |
| Bread          | Vegetable             | Bread                     |
|                | Bread                 | Canned fruit or ice cream |

Drink is divided into six portions—three with meals and three between meals and bedtime.

## 2. Recipe for Essenamine milk drink

|                    |                               |
|--------------------|-------------------------------|
| 60 Gm. corn starch | 4 teaspoons vanilla extract   |
| 150 Gm. Essenamine | $\frac{1}{2}$ teaspoon nutmeg |
| 40 Gm. brown sugar | 2 teaspoons cinnamon          |
| 100 Gm. corn syrup | 750 cc. milk                  |
| 1 egg              | 17.5 Gm. powdered malted milk |
| 3 Gm. salt         | 150 Gm. chocolate syrup       |
|                    | 500 cc. water                 |

Mix all ingredients except milk, egg and chocolate syrup. Cook until thick. Cool slightly, and add remaining ingredients. Blend at high speed for fifteen to twenty minutes. Serve chilled.

(Carbohydrate 276 Gm., protein 197 Gm., fat 47 Gm. and calories 2,315)

## B. High Essenaminc diet (160 Gm. of Essenaminc)

### 1. Menu

#### Breakfast

Orange

Oatmeal (20 Gm. of Essenaminc)

Muffin (10 Gm. of Essenaminc)

Fruit pudding (10 Gm. of Essenaminc)

Drink 250 cc. (16.67 Gm. of Essenaminc)

#### Lunch

Meat loaf (10 Gm. of Essenaminc)

Vegetable puree (10 Gm. of Essenaminc)

Muffin (10 Gm. of Essenaminc)

Pudding (10 Gm. of Essenaminc)

Drink 250 cc. (16.67 Gm. of Essenaminc)

#### Supper

Vegetable puree (10 Gm. of Essenaminc)

Fruit pudding (10 Gm. of Essenaminc)

Muffin (10 Gm. of Essenaminc)

Drink 250 cc. (16.67 Gm. of Essenaminc)

### 2 Recipes

#### (a) Drink

|                                 |                               |
|---------------------------------|-------------------------------|
| 3 Gm. agar dissolved in 40 cc.  | 25 Gm. tapioca flour          |
| boiling water                   | 15 Gm. vegetable oil          |
| 50 Gm. Essenaminc               | 2 Gm. salt                    |
| 35 Gm. brown sugar              | $\frac{1}{4}$ teaspoon nutmeg |
| $1\frac{1}{2}$ teaspoon vanilla | 720 cc. milk                  |
| $\frac{1}{2}$ egg               | Water if needed               |

Prepare as for aforementioned drink.

#### (b) Muffins (three for one day)

|                   |                                      |
|-------------------|--------------------------------------|
| 30 Gm. Essenaminc | $\frac{1}{3}$ teaspoon baking powder |
| 10 Gm. flour      | $\frac{1}{4}$ teaspoon salt          |
| 7 Gm. sugar       | $\frac{1}{2}$ teaspoon vanilla       |
| 1 egg             |                                      |
| 75 cc. water      |                                      |

Sift the dry constituents, add liquid and fold in the beaten white of egg. Bake in a moderate oven until done.

#### (c) Sauce for vegetable, soup or meat

|                   |  |
|-------------------|--|
|                   | 15 Gm. corn syrup                                      |
| 30 Gm. Essenaminc | 2 Gm. salt   |
| 5 Gm. oil         | $\frac{1}{2}$ teaspoon onion, celery or parsley flakes |
| 15 Gm. flour      | 200 cc. water  |

Mix all ingredients with water and cook over moderate flame until thick. Divide into three parts and use with vegetables, soup or meat.

(d) Sauce for fruit

40 Gm. Essenamaine    1 teaspoon cinnamon  
80 Gm. corn syrup    ½ teaspoon vanilla  
20 Gm. corn starch    Pinch nutmeg  
175 cc. water

Mix all ingredients together, and cook over medium flame until thick. Add 250 or 300 Gm. of fruit puree. Makes three servings.

(e) Meat loaf

75 Gm. ground beef  
5 Gm. onion  
5 Gm. oil

Mix with one third of the recipe for vegetable sauce. Bake in casserole.

Mrs. Hazel Parks, dietitian for the study, prepared all diets and recipes. Miss Shandus Pincoffs was her assistant. Miss Millie E. Kalsem, chief executive dietitian of the Cook County Hospital, cooperated and gave advice at all stages of the study.



## LOCALIZED PROXIMAL JEJUNITIS

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IN 1932, Crohn, Ginzburg and Oppenheimer<sup>1</sup> first described the clinicopathologic entity which was called "terminal ileitis." Since then, many instances of the same pathologic process in all parts of the ileum and jejunum have caused modification of the term to "regional enteritis." Of the numerous cases reported, however, in only a few has the disease been limited to the jejunum. Harris, Bell and Brunn<sup>2</sup> first described a case with the lesion wholly in the jejunum. Brown and Donald<sup>3</sup> included in their 178 cases of regional enteritis 5 instances of primary jejunal lesions. W. R. Johnson<sup>4</sup> reported a case with multiple diseased segments which were all confined to a few feet of jejunum and for which resection with end to side anastomosis was performed. H. N. Brewster<sup>5</sup> also described an instance of localized obstructing jejunitis in a small section of bowel treated by resection and anastomosis.

In the present report of a case, localized jejunitis, found at operation, involved approximately 10 inches (25 cm.) of jejunum but the upper limit was at the ligament of Treitz. On the basis of experience at the Mount Sinai Hospital, as reported by Garlock and Ginzburg,<sup>6</sup> which had demonstrated the effectiveness of simple ileocolostomy with exclusion but without resection in regional enteritis of the terminal portion of the ileum, the same principle was applied in the present case of enteritis localized to the jejunum.

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From the Surgical Service, Mount Sinai Hospital.

1. Crohn, B. B.; Ginzburg, L., and Oppenheimer, G. D.: Regional Ileitis: Pathologic and Clinical Entity, *J. A. M. A.* **99**:1323 (Oct. 15) 1932.

2. Harris, F. I.; Bell, G. H., and Brunn, H.: Chronic Cicatrizing Enteritis: Regional Ileitis (Crohn) New Surgical Entity, *Surg., Gynec. & Obst.* **57**:637 (Nov.) 1933.

3. Brown, P. W., and Donald, C. J.: Prognosis of Regional Enteritis, *Am. J. Digest. Dis.* **9**:87 (March) 1942.

4. Johnson, W. R.: Chronic, Non-Specific Jejunitis with Unusual Features, *Gastroenterology* **1**:347 (April) 1943.

5. Brewster, H. N., cited by Crohn, B. B., in discussion on Johnson.<sup>4</sup>

6. Garlock, J. H., and Ginzburg, L.: Regional Ileitis, *Ann. Surg.* **116**:906 (Dec.) 1942.

Accordingly, the lesion was short circuited by transecting of the jejunum distal to the lower limits of the jejunitis and performing of a side to side duodenojejunostomy between the third portion of the duodenum and the jejunum, which had been severed distal to the lesion. The patient's postoperative course was uneventful, his symptoms disappeared and he has remained well in the three year interval since operation.



Roentgenogram showing the typical "string" sign confined to the proximal 10 inches of jejunum. The lesion is sharply demarcated.

#### REPORT OF A CASE

*History.*—A. N., a 30 year old white Jewish man, was admitted to the Mount Sinai Hospital on Oct. 25, 1943, with a three year history of intermittent, para-umbilical, dull and boring pain, occurring often, but not invariably, after eating and lasting from five minutes to a half-hour. There was no nausea, vomiting or change in bowel habit. Roentgenologic studies in the Army showed "some abnormality of the small intestinal pattern," but after a tentative diagnosis of nontropical sprue the patient was finally considered to be psychoneurotic and was discharged from the service.

Following discharge, the pains increased in intensity and frequency and were often associated with nausea and vomiting. Appetite declined, and the patient lost 30 pounds (13 Kg.). Both appetite and weight were partially regained on a regimen which included parenteral administration of vitamin B complex and insulin. Radiation therapy to the abdomen seemed to lessen the degree and frequency of pain. However, the symptoms continued severely enough to prevent the patient from working.

Finally, careful roentgenologic studies of the small bowel showed a localized area of constriction in the jejunum, starting at the duodenojejunal junction and extending for about 10 inches (fig. 1).

*Examination.*—The patient was thin and showed evidence of loss of weight but was not dehydrated. The temperature was 99.6 F. and the pulse rate 84. There were no other significant physical findings except slight tenderness in the midline of the upper part of the abdomen, just above the umbilicus. No masses were palpable.

*Laboratory Data.*—The hemoglobin content (Sahli) was 83 per cent, red blood cell count 4,800,000 and white blood cell count 5,600, with segmented polymorphonuclears 55 per cent, nonsegmented polymorphonuclears 20 per cent, lymphocytes 21 per cent, monocytes 3 per cent and eosinophils 1 per cent.

The urine gave an alkaline reaction; specific gravity was 1.010; examinations for albumin and sugar and microscopic examination gave normal results.

*Operation* (Dr. John H. Garlock).—On Oct. 26, 1943, with the patient under ethylene-ether anesthesia, a midrectus muscle-splitting incision was made on the right side. The jejunum, beginning at the ligament of Treitz and extending for a distance of 10 inches, was decidedly reddened, and the wall was thickened. The mesentery of the inflamed segment of jejunum was edematous and contained several large lymph nodes. The area of involvement of the intestine ended sharply. The remainder of the entire small intestine was carefully inspected and found to be normal.

Six inches (15 cm.) distal to the lower border of the jejunitis, the jejunum was transected and each end inverted with three layers of silk. The distal limb was brought up beneath the transverse colon to the third portion of the duodenum. A side to side duodenojejunostomy was made, fine chromic surgical gut being used on the mucosal layers and fine silk for the serosal surfaces. The wound was closed with buried, interrupted figure of eight, steel alloy wire sutures. The skin was approximated with clips.

*Course.*—The postoperative course was uneventful except for a gradual rise in temperature, reaching 102 F. on the third day. The temperature was normal by the seventh day, where it remained until the patient was discharged, thirteen days after operation. The bowels were moving normally every other day at the time the patient left the hospital.

*Follow-up.*—The patient has had no recurrence of intestinal symptoms and has gained weight. At the last visit his general condition was excellent and his abdomen nontender.

#### SUMMARY

This is the first reported instance of localized jejunitis treated by a short-circuiting procedure without resection.

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